Electronic Supplementary Information

Screening of metal ions and organocatalysts on solid support-coupled DNA oligonucleotides guides design of DNA-encoded reactions

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General methods and materials

Unless otherwise noted, chemicals were purchased from *abcr, Acros Organics, Alfa Aesar, Fisher Scientific, Merck, Sigma Aldrich, TCI* and *VWR* and were used as provided without further purifications. Dry solvents (CH_2Cl_2, DMF, MeOH, ACN, EtOH, THF, toluene) were used as commercially available.

5'-Aminolinker-modified DNA oligonucleotides coupled to controlled pore glass solid support (CPG, 1000 Å porosity) were synthesized by *IBA* (Göttingen, Germany). Oligonucleotide-small molecule conjugates coupled to CPG were filtered and washed through synthesis columns using a vacuum manifold (*Vac-Man*®) from *Promega*.

Semi-preparative ion pair RP-HPLC. Compound purification was performed on a *Shimadzu Prominence* HPLC System equipped with a C_{18} stationary phase (*Phenomenex*, Gemini, 5 µm, C_{18}, 110 Å, 100 x 4.6 mm). A gradient from 100 mM aqueous triethylammonium acetate (pH = 8.0, eluent A) to MeOH (eluent B) was used at a flow rate of 5 mL/min. Fractions containing the desired product were pooled and concentrated.

> **Method:** Step gradient of 20 % to 70 % B within 13 min, then 70 % to 100 % B within 1 min followed by 100 % B for 3 min using 100 mM aqueous triethylammonium acetate (pH = 8.0, eluent A) and MeOH (eluent B) at a flow rate of 5 mL/min.

Analytical RP-HPLC. HPLC analysis was performed on an *Agilent 1100 series* chromatograph equipped with 1100 Quaternary Pump (*G1311A*), a 1100 Multi-Wavelength Detector (*G1365B*) and an *Agilent Eclipse Plus* C_{18} (4.6 x 100 mm, 3.5 µm) column. The conversion and purity of DNA conjugates were determined by integration of peaks recorded at 254 nm wavelength.

> **Method-I:** Step gradient of 10 % to 60 % B within 10 min, then 60 % to 100 % B within 2 min followed by 100 % B for 2 min using 10 mM aqueous triethylammonium acetate (pH = 8.0, eluent A) and MeOH (eluent B) at a flow rate of 0.6 mL/min.
>
> **Method-II:** Step gradient of 10 % to 70 % B within 10 min, then 70 % to 100 % B within 2 min followed by 100 % B for 2 min using 10 mM aqueous triethylammonium acetate (pH = 8.0, eluent A) and MeOH (eluent B) at a flow rate of 0.6 mL/min.
>
> **Method-III:** A linear gradient of 10 % to 100 % B within 10 min followed by 100 % B for 4 min using 10 mM aqueous triethylammoinum acetate (pH 8.0, eluent A) and MeOH (eluent B) at a flow rate of 0.6 mL/min.

MALDI-TOF. Mass analysis was performed on a MALDI TOF/TOF MS from *Bruker Daltonics* using 2',4',6'-trihydroxyacetophenone (THAP) matrix (*Dichrom*).

Representative procedures

DMT-deprotection and capping of solid support-coupled hexT (RP_01)

The DMT-protecting group of 5'-amino linker modified hexT-DNA strand coupled to 1000 Å controlled pore glass (CPG) solid support (1 µmol, ca. 36 mg) was cleaved by addition of 3% trichloroacetic acid in CH_2Cl_2 (3x 200 µL) for 1 min (yellow to orange color indicated successful removal of protecting group). The CPG was washed with DMF (3x 200 µL), MeOH (3x 200 µL), ACN (3x 200 µL) and CH_2Cl_2 (3x 200 µL). Deprotected CPG-coupled oligonucleotide was treated with 200 µL of capping solution (1:1 mixture of THF/methylimidazole (9:1, vol:vol) and THF/pyridine/acetic acid anhydride (8:1:1, vol/vol)) for 1 min. Finally, the CPG was washed three times with each 200 µL of DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo* for 15 min. Capping was repeated three times.

To assess completion of deprotection and capping, a small portion of CPG (0.7 mg) was treated with 500 µL of an AMA solution (AMA = aqueous ammonia (30%)/ aqueous methylamine (40%), 1:1, vol/vol) for 30 min at room temperature. Afterwards 20 µL if 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and dissolved in 100 µL of distilled water. The product was analyzed by Analytical RP-HPLC and MALDI-TOF-MS.

DMT-deprotection of solid support-coupled 10mer DNA strands (RP_02)

The DMT-protecting group of DNA strand coupled to 1000 Å controlled pore glass (CPG) solid support (1 µmol, ~40 mg of 10mer DNA (TC-, ATC-, ATCG-Sequences)) was cleaved by addition of 3% trichloroacetic acid in CH_2Cl_2 (3x 200 µL) for 1 min (yellow to orange color indicated successful removal of protecting group). The CPG was washed three times with each 200 µL of DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo* for 15 min.

Treatment of solid support-coupled DNA with metal salts (RP_03)

20 nmol of CPG-coupled oligonucleotide (ca. 0.7 mg solid phase) were treated with 200 equiv. of metal salt (4 µmol) dissolved in 50 µL dry solvent. The suspension was shaken at ambient temperature for 22 h. Afterwards the solvent was removed by filtration, and the CPG was washed three times with each 200 µL of 0.1 M EDTA solution, 0.1 M $MgCl_2$ solution, water, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*.

Cleavage and analysis: DNA was deprotected and cleaved from CPG by shaking with 500 µL of an AMA solution (AMA = aqueous ammonia (30%)/ aqueous methylamine (40%), 1:1, vol/vol)

for 4 h (30 min for hexT-Ac) at room temperature. Afterwards, 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and the DNA was dissolved in 200 µL distilled water. The product was analyzed by Analytical RP-HPLC and MALDI-TOF-MS.

Treatment of solid support-coupled DNA with organocatalysts (RP_04)

20 nmol of CPG-coupled oligonucleotide (ca. 0.7 mg of solid phase) were treated with 200 equiv. of organocatalyst (4 µmol) dissolved in 50 µL dry solvent. The suspension was shaken at ambient temperature for 22 h. Afterwards, the solvent was removed by filtration, the CPG was washed three times with each 0.1 M $MgCl_2$ solution, water, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*.

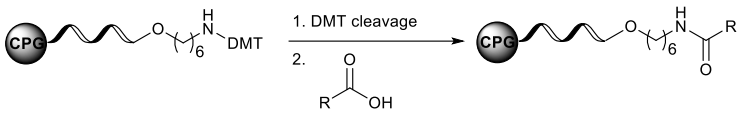
Cleavage and analysis: DNA was deprotected and cleaved from CPG by shaking in 500 µL of an AMA solution (AMA = aqueous ammonia (30%)/ aqueous methylamine (40%), 1:1, vol/vol) for 4 h (30 min for hexT-Ac) at room temperature. Afterwards 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and DNA was dissolved in 200 µL distilled water. The product was analyzed by Analytical RP-HPLC and MALDI-TOF-MS.

Treatment of solid support-coupled DNA with acids (RP_05)

20 nmol of CPG-coupled oligonucleotide (ca. 0.7 mg of solid phase) were treated with 50 µL acid. The suspension was shaken at ambient temperature for 22 h. Afterwards solution was removed by filtration, and the CPG was washed three times with each 200 µL of 0.1 M $MgCl_2$ solution, water, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*.

Cleavage and analysis: DNA was deprotected and cleaved from CPG by shaking in 500 µL of an AMA solution (AMA = aqueous ammonia (30%)/ aqueous methylamine (40%), 1:1, vol/vol) for 4 h (30 min for hexT-Ac) at room temperature. Afterwards 20 µL if 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and dissolved in 200 µL of distilled water. The product was analyzed by Analytical RP-HPLC and MALDI-TOF-MS.

Amide coupling (RP-06)



Step 1: The DMT-protecting group of CPG-coupled oligonucleotide (250 nmol, ca. 10 mg of solid phase material) was removed by addition of 200 µL 3 % trichloroacetic acid in CH_2Cl_2 for 1 min. Orange coloring of the solution indicated successful removal of protecting group. The deprotection was repeated 3-5 times until no further coloring of the solution was observed. The CPG-coupled deprotected DNA was washed three times with each 200 µL of 1 % TEA in ACN, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*.

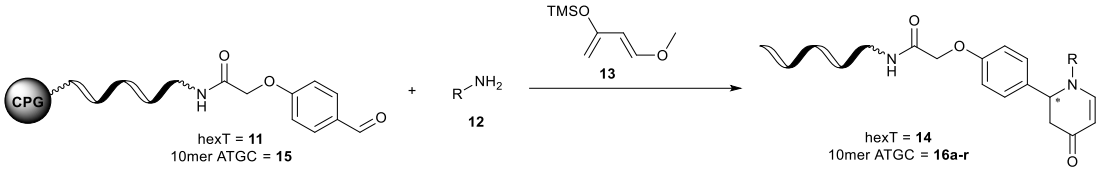
Step 2:

CPG-coupled oligonucleotide, carboxylic acid and HATU were dried *in vacuo* for 15 min. Stock solutions of all reactants in dry DMF were prepared before the reaction was started. To the solution of carboxylic acid (25 µmol, 100 equiv.) in 75 µL dry DMF, HATU (25 µmol, 100 equiv.) dissolved in 75 µL dry DMF and DIPEA (62.5 µmol, 250 equiv.) were added. The mixture was shaken for 5 min and added to CPG-coupled DNA suspended in 75 µL dry DMF (250 nmol, 1 equiv.). The amide coupling reaction was shaken at ambient temperature for 2 hours. Next, the CPG-coupled conjugate was filtered over a filter column, washed three times with each 200 µL of DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*. Amide coupling was repeated two times.

Completion of amide coupling was controlled by cleaving off a small portion of CPG-coupled oligonucleotide conjugate (0.7–0.9 mg, ~20 nmol) with 500 µL AMA (AMA = aqueous ammonia (30 %)/ aqueous methylamine (40 %), 1:1, vol/vol) for 30 min (hexT) or 4 h (ATGC-sequences) at ambient temperature. Afterwards 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and DNA was dissolved in 200 µL distilled water. The crude reaction mixture was analyzed by analytical RP-HPLC and MALDI-MS. In case of uncompleted coupling (<90%) the reaction was repeated a third time.

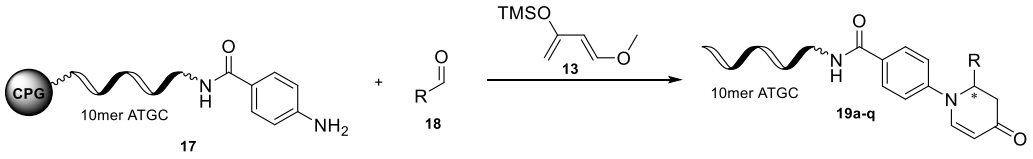
Unreacted amines were capped with acetic acid anhydride (three times 200 µL, 30 s, 1:1 mixture of THF/methylimidazole, 9:1, vol/vol, and THF/pyridine/acetic acid anhydride 8:1:1, vol/vol). The capped CPG-coupled oligonucleotide conjugate was washed three times with each 200 µL of DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*.

aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled oligonucleotide-aldehyde conjugates (RP-07)



Prior to reaction, CPG-coupled oligonucleotide, solid amines and $ZnCl_2$ were dried *in vacuo* for 15 min. Amine **14** (10 µmol, 500 equiv.) was dissolved in 24 µL acetonitrile. The solution was added to CPG-coupled oligonucleotide-aldehyde conjugate **13** (20 nmol) suspended in 12 µL triethyl orthoformate. The suspension was shaken at ambient temperature for 4 h. Afterwards 30 µL of $ZnCl_2$ (2 µmol, 100 equiv.) in ACN followed by Danisheskys's diene **15** (20 µmol, 1000 equiv.) was added. The reaction mixture was shaken for 1 h at ambient temperature. Then the CPG-coupled oligonucleotide conjugate was filtered over a filter column, washed three times with each 200 µL of 0.1 M EDTA solution, 0.1 M $MgCl_2$ solution, water, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*. CPG-coupled oligonucleotide conjugates **16-19** (**16** = hexT, **18** = 10mer ATGC) were cleaved from solid support and deprotected with 200 µL aqueous ammonia (30 %) at 50 °C for 6 h. Afterwards 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and DNA was dissolved in 200 µL distilled water. The crude reaction mixture was analyzed by analytical RP-HPLC (Method I) and MALDI-TOF-MS. The product was purified by preparative RP-HPLC.

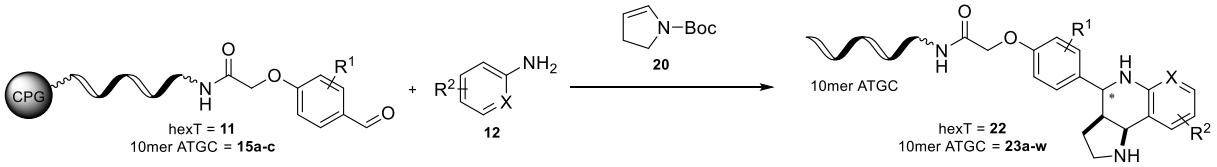
aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled oligonucleotide-aniline conjugates (RP-08)



Prior to reaction, CPG-coupled oligonucleotide, solid aldehydes and $ZnCl_2$ were dried *in vacuo* for 15 min. Aldehyde **14** (30 µmol, 1500 equiv.) was dissolved in 24 µL tetrahydrofuran. The solution was added to CPG-coupled oligonucleotide-aniline conjugate **13** (20 nmol) suspended in 12 µL triethyl orthoformate. The suspension was shaken at ambient temperature for 4 h. Afterwards 30 µL of $ZnCl_2$ (2 µmol, 100 equiv.) in tetrahydrofuran followed by Danishefsky's diene **15** (20 µmol, 1000 equiv.) were added. The reaction mixture was shaken at ambient temperature for 1 h. Then the CPG-coupled oligonucleotide conjugate was filtered over a filter column, washed three times with each 200 µL of 0.1 M EDTA solution, 0.1 M $MgCl_2$ solution,

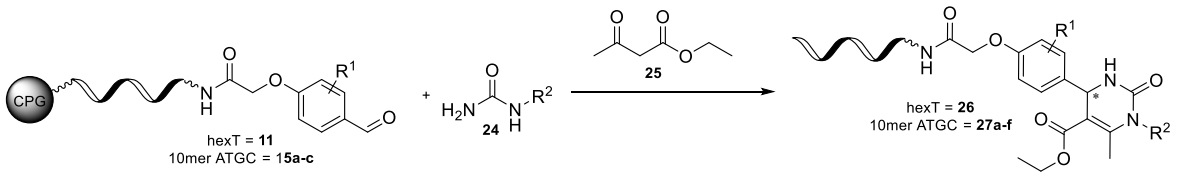
water, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*. CPG-coupled oligonucleotide conjugates **16** and **19** (**16** = hexT, **19** = 10mer ATGC) were cleaved from solid support and deprotected with 200 µL aqueous ammonia (30 %) at 50 °C for 6 h. Afterwards, 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and DNA was dissolved in 200 µL distilled water. The crude reaction mixture was analyzed by analytical RP-HPLC (Method I) and MALDI-TOF-MS. The product was purified by preparative RP-HPLC.

(*R*)-(-)-BNDHP-mediated Povarov reaction on CPG-coupled oligonucleotides (RP-09)



Prior to use, CPG-coupled oligonucleotide, solid anilines and (*R*)-(-)-BNDHP were dried *in vacuo* for 15 min. Aniline **12** (10 µmol, 500 equiv.) was dissolved in 24 µL ethanol. The solution was added to CPG-coupled oligonucleotide-aldehyde conjugate **15** (20 nmol) suspended in 12 µL triethyl orthoformate. The suspension was shaken at ambient temperature for 4 h. Afterwards 30 µL of (*R*)-(-)-BNDHP (2 µmol, 100 equiv.) in ethanol followed by *N*-Boc-2,3-dihydro-1H-pyrrole **20** (10 µmol, 500 equiv.) were added. The reaction mixture was shaken at 50 °C for 16 h. Then the CPG-coupled oligonucleotide conjugate was filtered over a filter column, washed three times with each DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*. Boc-protecting group was removed by addition of 200 µL 75 % trifluoroacetic acid in CH_2Cl_2 for 30 sec.. Afterwards CPG-coupled DNA was washed with excess of 1 % TEA and CH_2Cl_2. The deprotection was repeated 4 times. The solid phase was washed three times with each 200 µL of 1 % TEA in ACN, DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*. CPG-coupled oligonucleotide conjugates **22-23** were cleaved from solid support and deprotected with 500 µL AMA (AMA = aqueous ammonia (30 %)/ aqueous methylamine (40 %), 1:1, vol/vol) for 30 min (hexT **22**) or 4 h (ATGC-sequences **23**) at ambient temperature. Afterwards 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and DNA was dissolved in 200 µL distilled water. The crude reaction mixture was analyzed by analytical RP-HPLC (Method I) and MALDI-TOF-MS. The product was purified by preparative RP-HPLC.

(*R*)-(-)-BNDHP-mediated Biginelli reaction on CPG-coupled oligonucleotides (RP-10)



Prior to reaction, CPG-coupled oligonucleotide, ureas and (*R*)-(-)-BNDHP were dried *in vacuo* for 15 min. Urea **24** (10 µmol, 500 equiv.) and (*R*)-(-)-BNDHP (1 µmol, 50 equiv.) were dissolved both in 30 µL ethanol. The solutions were added to CPG-coupled oligonucleotide-aldehyde conjugate **15** (20 nmol) followed by ethyl acetoacetate **25** (10 µmol, 500 equiv.). The reaction mixture was shaken at 50 °C for 20 h. Then the CPG-coupled oligonucleotide conjugate was filtered over a filter column, washed three times with each DMF, MeOH, ACN and CH_2Cl_2 and dried *in vacuo*. CPG-coupled oligonucleotide conjugates **26-27** were cleaved from solid support and deprotected with 500 µL AMA (AMA = aqueous ammonia (30 %)/ aqueous methylamine (40 %), 1:1, vol/vol) for 30 min (hexT **26**) or 4 h (ATGC-sequences **27**) at ambient temperature. Afterwards 20 µL of 1 M Tris buffer (pH = 7.5) were added, the mixture was dried under reduced pressure (SpeedVac) and DNA was dissolved in 200 µL distilled water. The crude reaction mixture was analyzed by analytical RP-HPLC (Method I) and MALDI-TOF-MS. The product was purified by preparative RP-HPLC.

Investigation in the stability of solid phase coupled oligonucleotides charged with metal ions and organocatalysts

Table S1 – Stability of DNA against metal salts[a]

Entry	Metal salt	Solvent	hexT-Ac	TC	ATC	ATCG
1	2% TFA					
2	10% TFA					
3	3.7% HCl					
4	AgOAc	CH_2Cl_2				
5	AgOTf	ACN				
6	$AgSbF_6$	ACN				
7[b]	$BiBr_3$	ACN				
8	$Bi(OTf)_3$	MeOH				
9	$Ce(NH_4)_2(NO_3)_6$	MeOH				
10	$Co(acac)_3$	ACN				
11[b]	CuCl	MeOH				
12	$Cu(MeCN)_4PF_6$	ACN				
13	$Cu(OTf)_2$	ACN				
14	$Fe(acac)_3$	ACN				
15	$FeCl_2 \bullet 4\ H_2O$	ACN				
16	$InCl_3$	ACN				
17[b]	La(O*i*-Pr)$_3$	THF				
18	LiBr	ACN				
19	$Mg(ClO_4)_2$	MeOH				
20	$Ni(acac)_2$	ACN				
21	$Ni(PPh_3)_2Cl_2$	MeOH				
22[b]	$Pd(dba)_3$	MeOH				
23a	$Pd(OAc)_2$	ACN				
23b[c]	$Pd(OAc)_2$	ACN				
24[c]	$Pd(PPh_3)_4$	MeOH				
25[b]	$[Rh(cod)Cl]_2$	MeOH				
26	$RuCl_3$	ACN				
27	$[Ru(p\text{-cymene})Cl_2]_2$	CH_2Cl_2				
28	$Ru(Me\text{-}allyl)_2(COD)$	CH_2Cl_2				
29	Grubbs 1st Gen.	CH_2Cl_2				
30	$SbCl_3$	ACN				
31	$Sc(OTf)_3$	ACN				
32	SeO_2	MeOH				
33	Ti(O*i*-Pr)$_4$	MeOH				
34	$VO(acac)_2$	MeOH				
35	$Yb(OTf)_3$	MeOH				
36	$ZnCl_2$	ACN				

[a] for each: 20 nmol DNA, 200 eq. transition metal salt, 50 µL solvent, r.t., 22 h. [b] poor solubility, added as suspension.
[c] 5 equiv. of metal salt were used.. ACN = acetonitrile, MeOH = methanol, THF = tetrahydrofuran.

0-20%	21-40%	41-60%	> 61%	DNA degradation

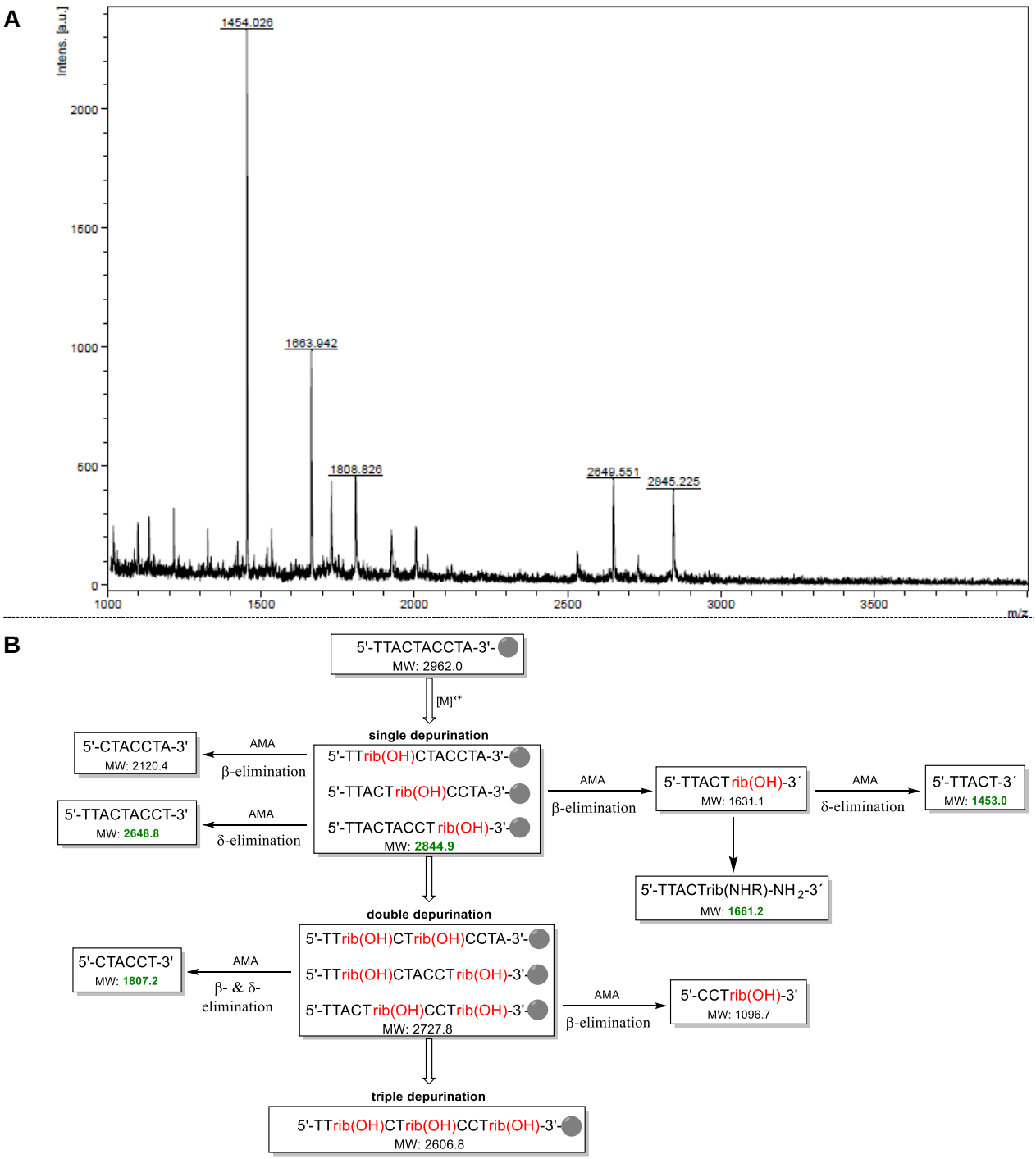
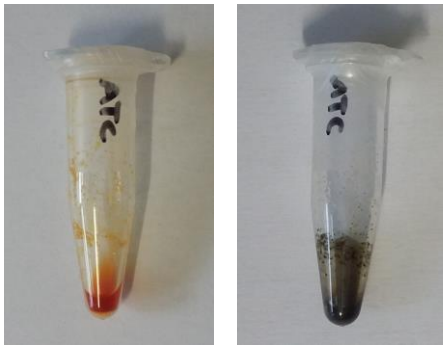


Figure S1 Representative mass spectrometric analysis of degraded DNA. A: MALDI-TOF spectrum for 10mer ATC-oligonucleotide **9** after treatment with aqueous 3.7% HCl. B: Possible depurination and fragmentation products of 10mer ATC-oligonucleotide **9**.

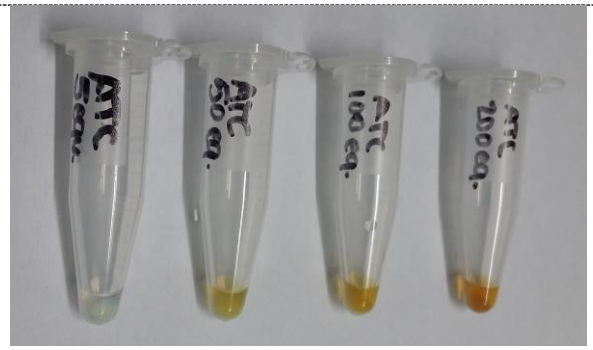
A



$Pd(PPh_3)_4$, 3 h $Pd(PPh_3)_4$, 22 h

Colouring of the $Pd(PPh_3)_4$ solution indicated redox processes which are plausible as all experiments were performed without protective gas.

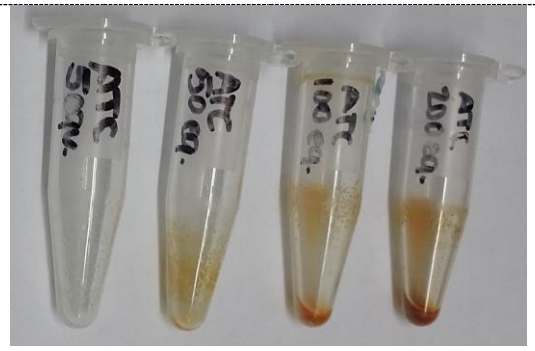
B



5 equiv. 50 equiv. 100 equiv. 200 equiv.

CPG-coupled DNA suspended in a solution of x equiv. $Pd(OAc)_2$ for 0 h at ambient temperature.

C



5 equiv. 50 equiv. 100 equiv. 200 equiv.

CPG-coupled DNA suspended in a solution of x equiv. $Pd(OAc)_2$ for 22 h at ambient temperature.

D

5 equiv. 50 equiv. 100 equiv. 200 equiv.

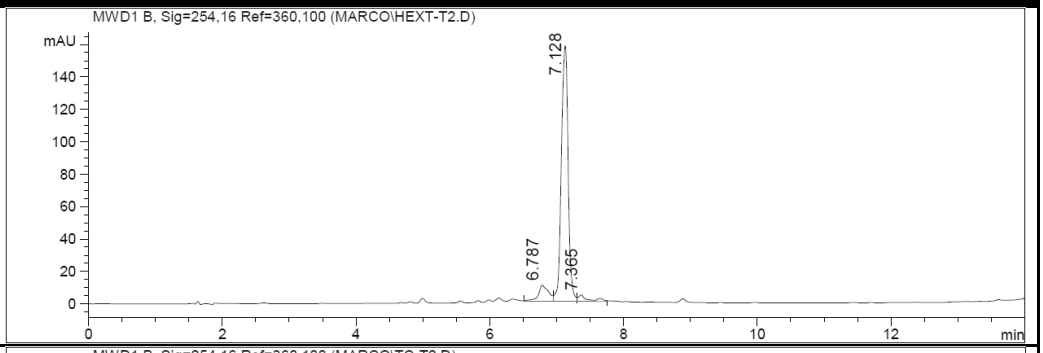
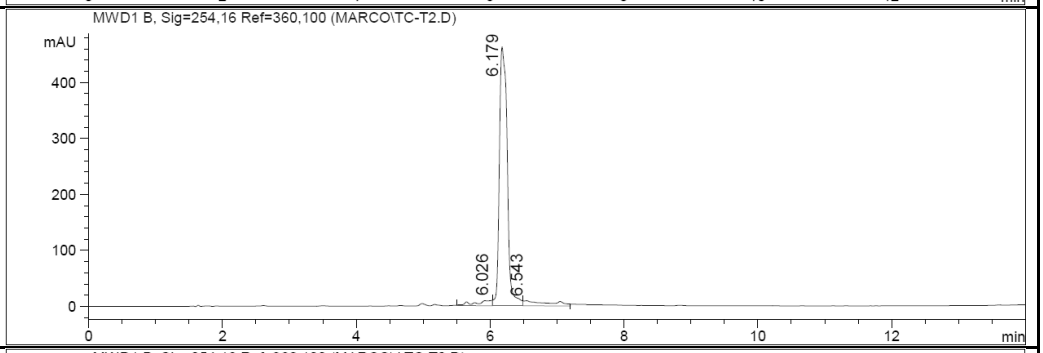
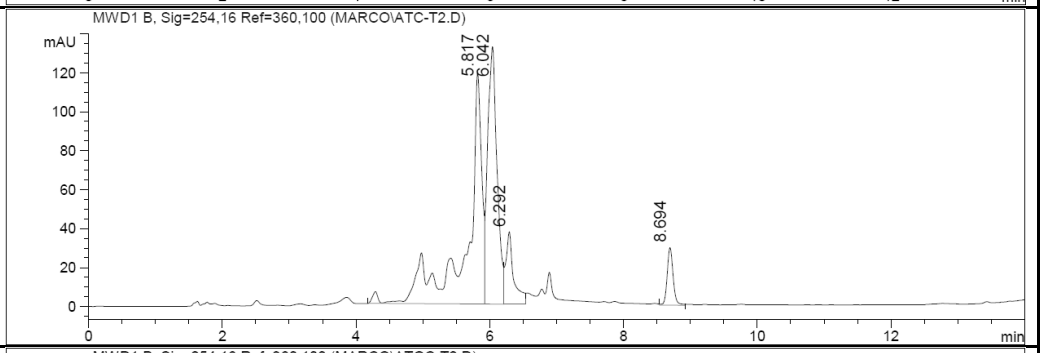
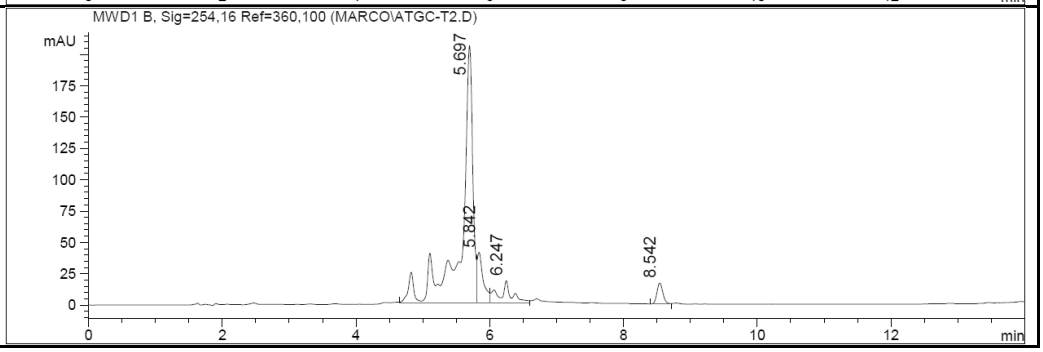
CPG-coupled DNA after incubation with a solution of x equiv. $Pd(TFA)_2$, for 22 h at ambient temperature and multiple washing steps. Slight coloring of CPG treated with higher amounts of $Pd(OAc)_2$ is observable.

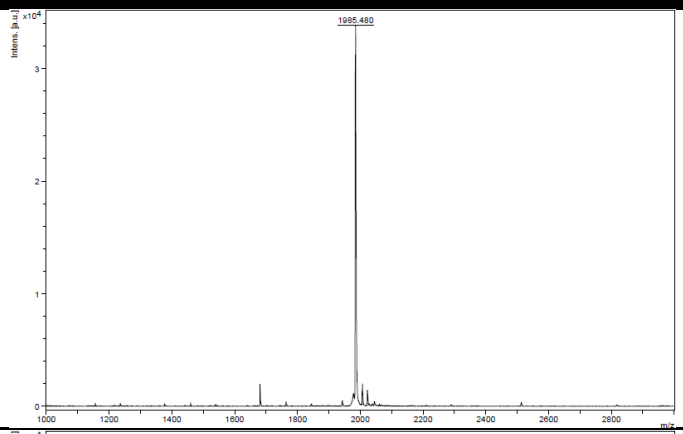
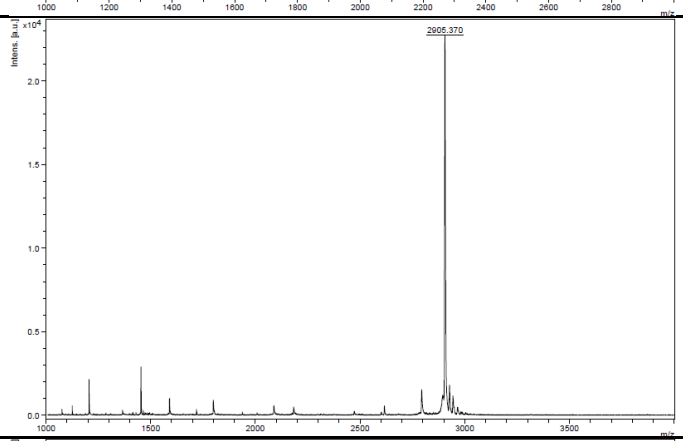
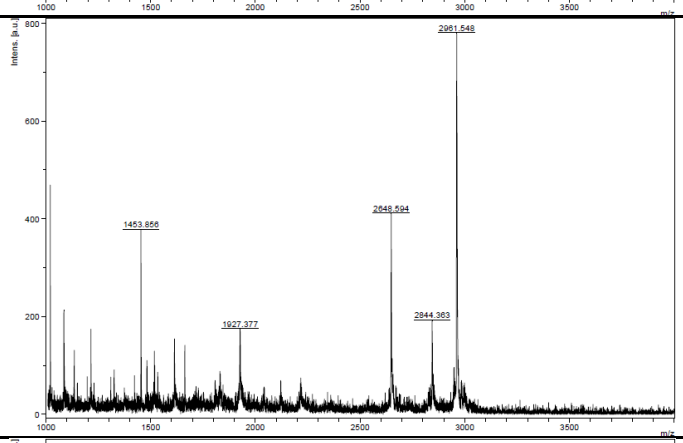
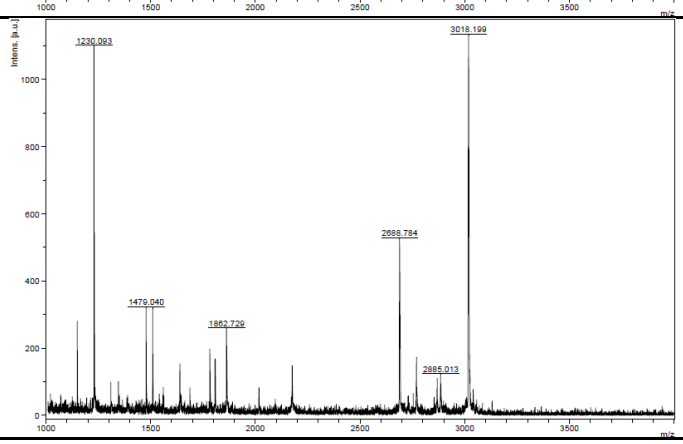
Figure S2 Photos of CPG-coupled DNA-oligonucleotides treated with Pd(O) and Pd(II).

HPLC traces and MALDI-MS spectra of metal ion screens

CPG-oligonucleotide + 2% TFA

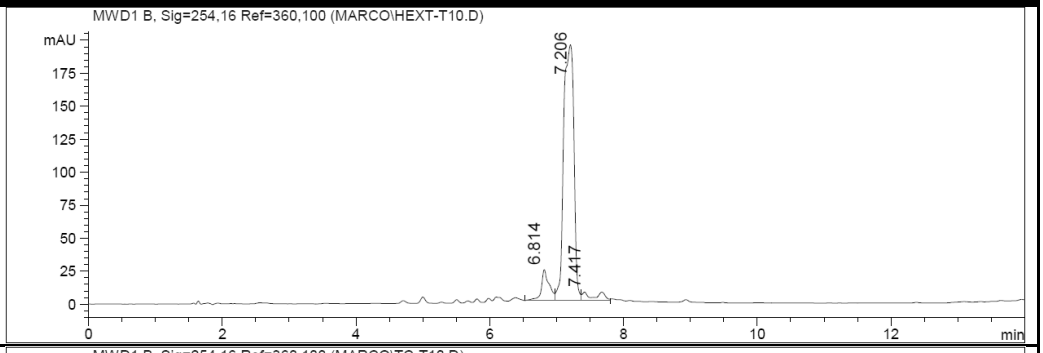
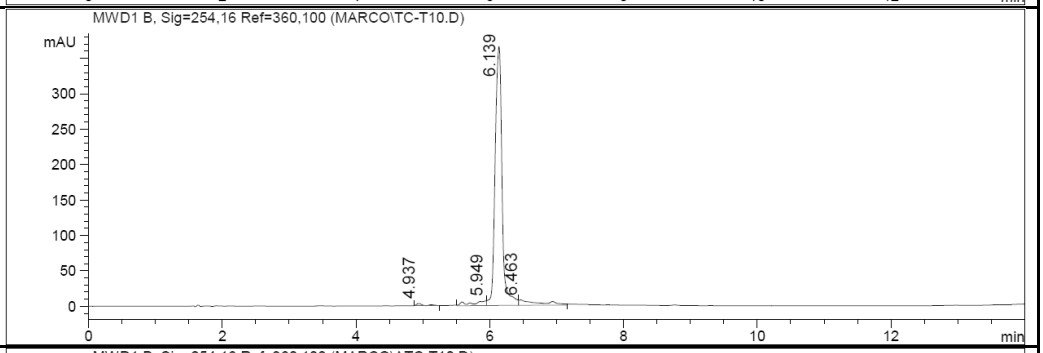
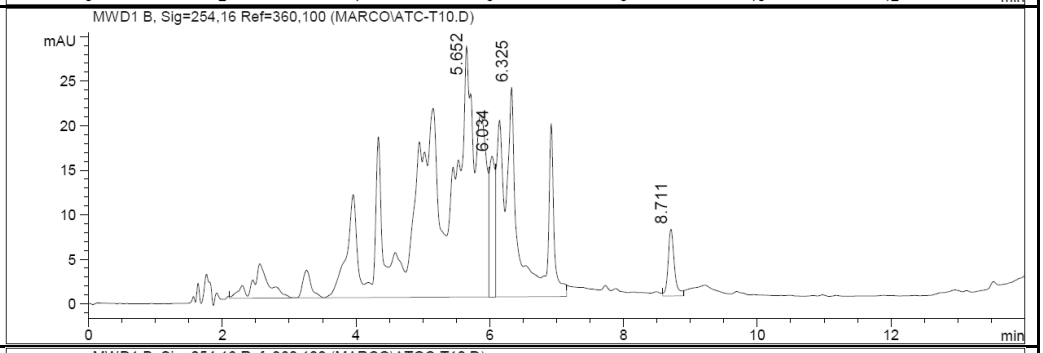
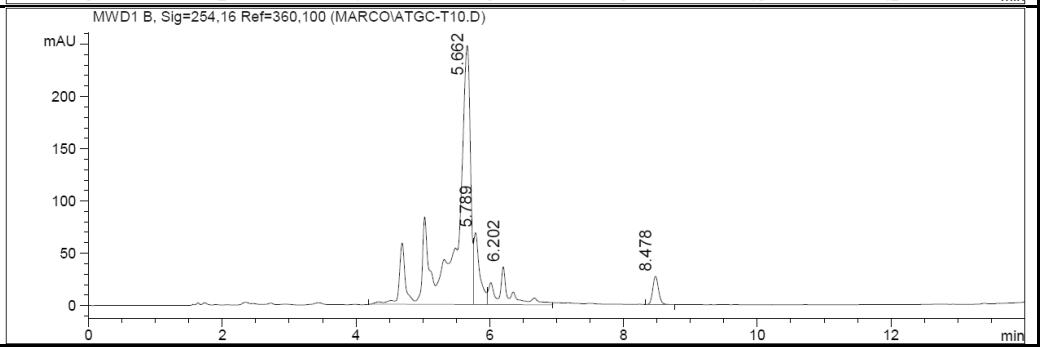
According to the representative procedure (RP-05) solid support coupled oligonucleotide (20 nmol) was treated with 2% TFA.

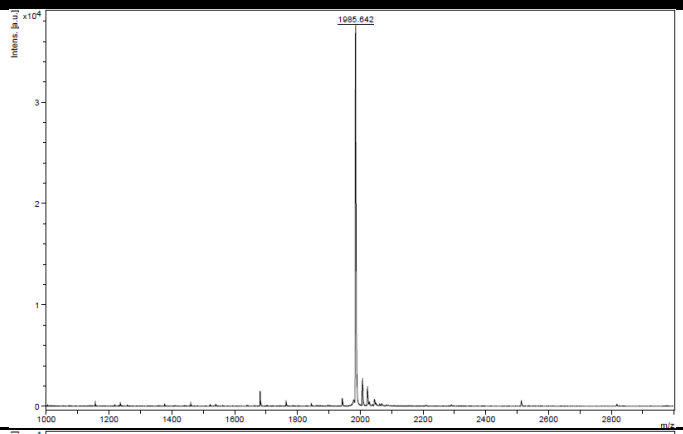
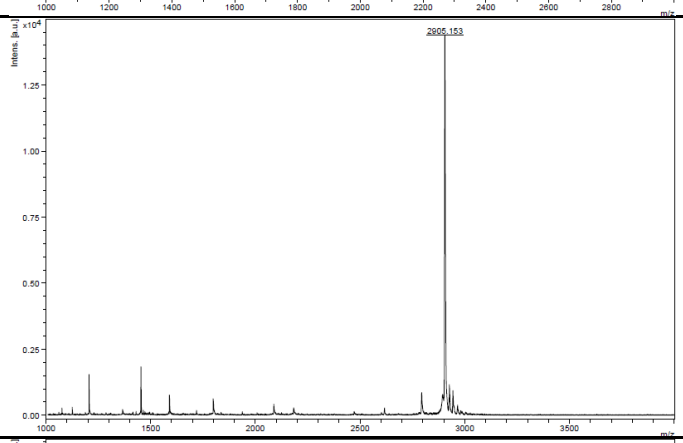
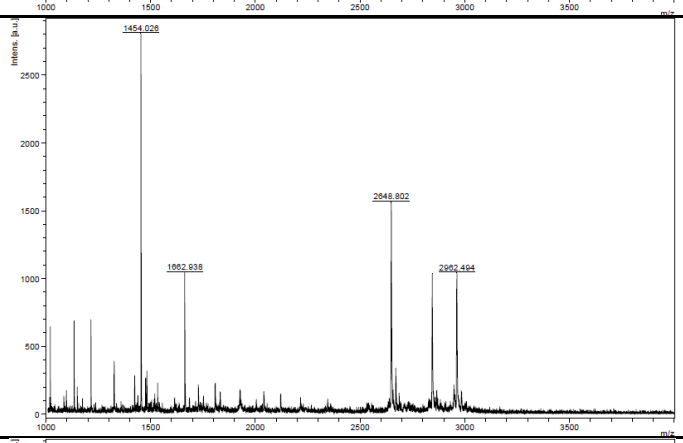
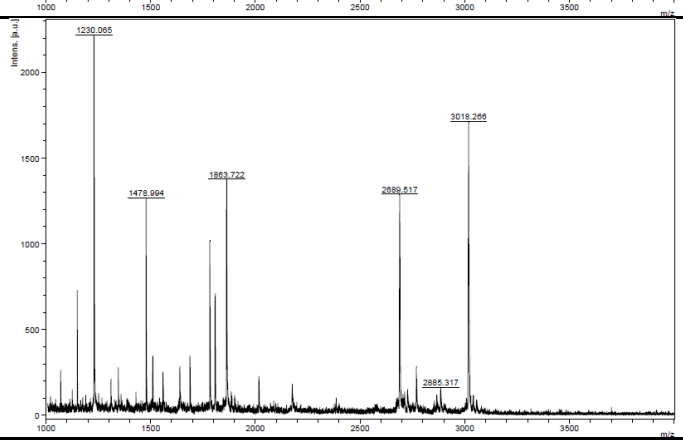
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.5
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.6
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.2

CPG-oligonucleotide + 10 % TFA

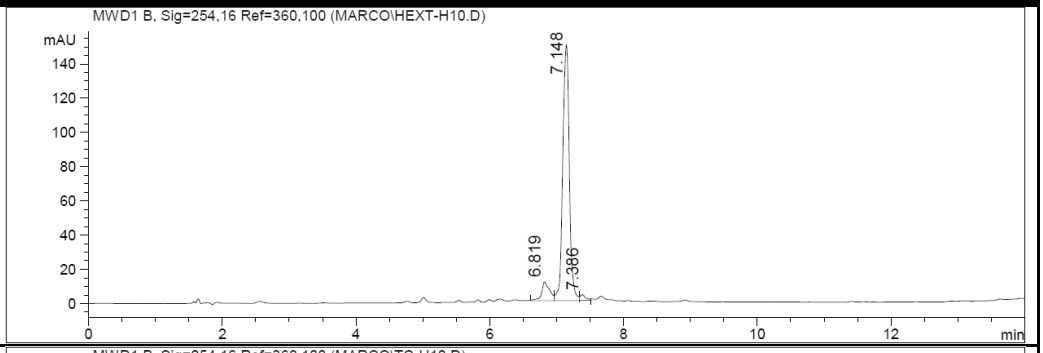
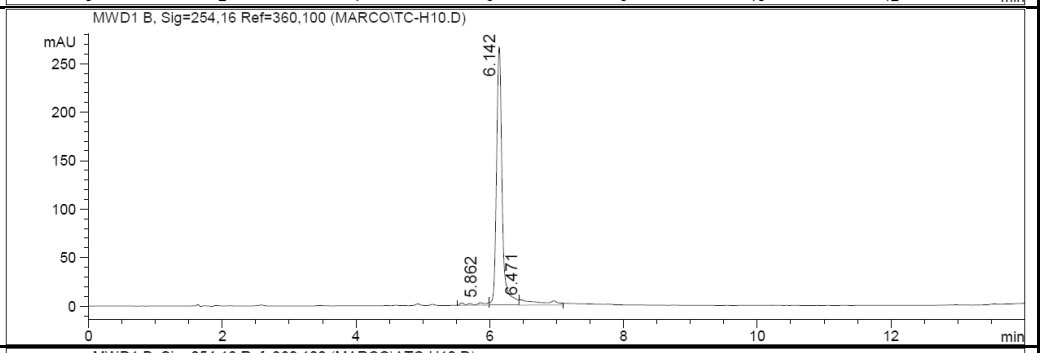
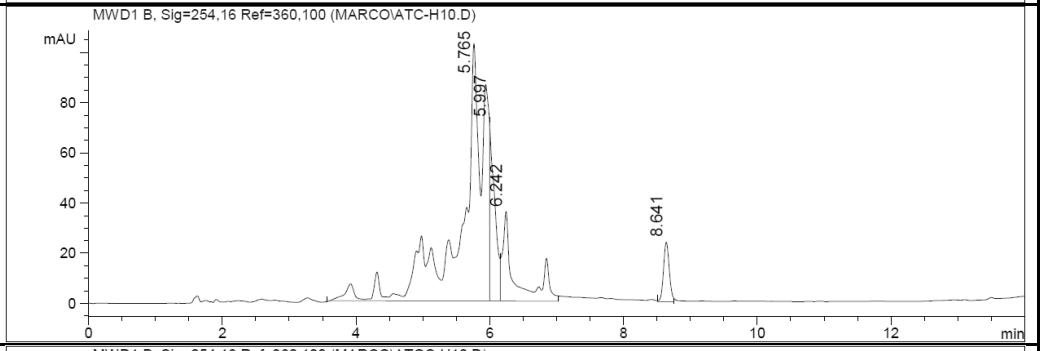
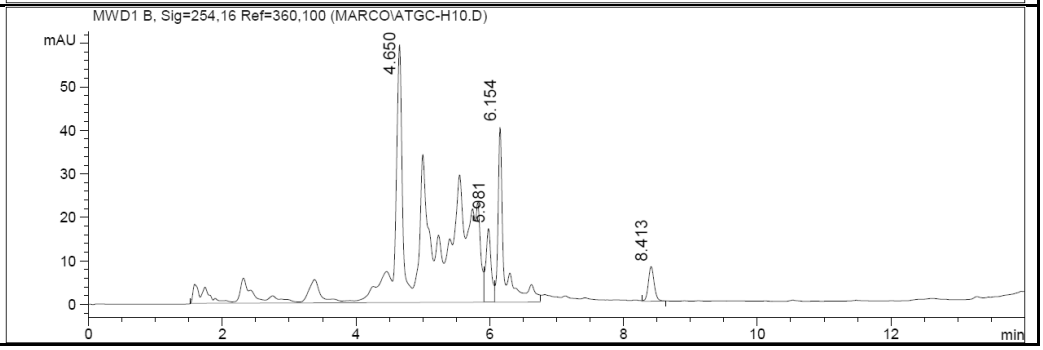
According to the representative procedure (RP-05) solid support coupled oligonucleotide (20 nmol) was treated with 10 % TFA.

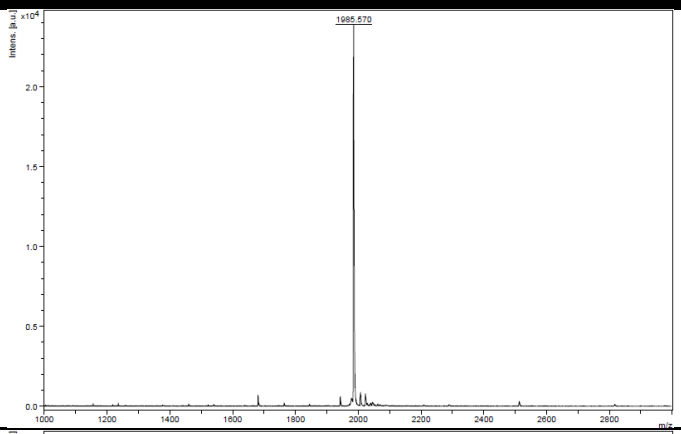
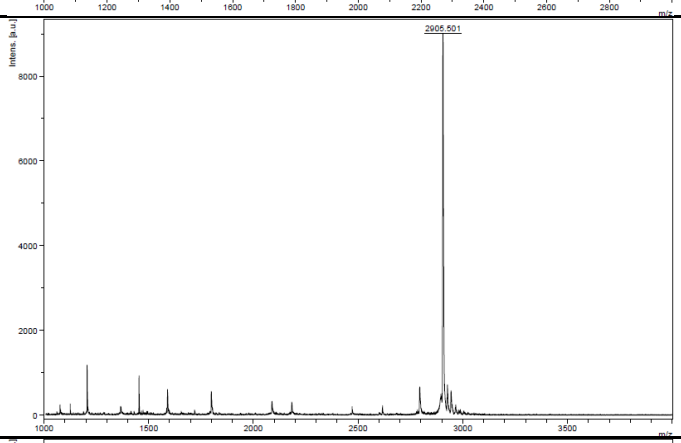
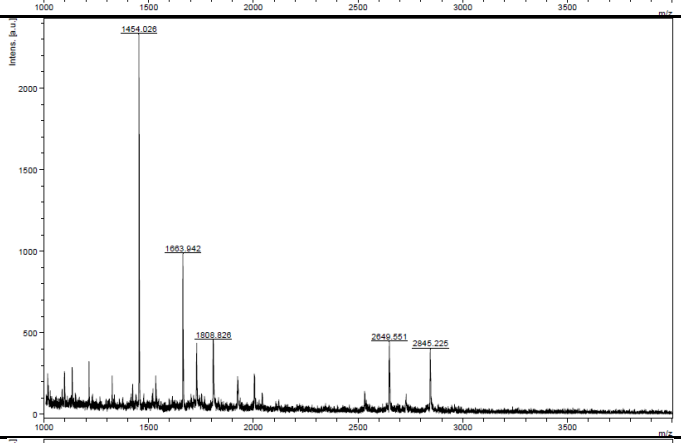
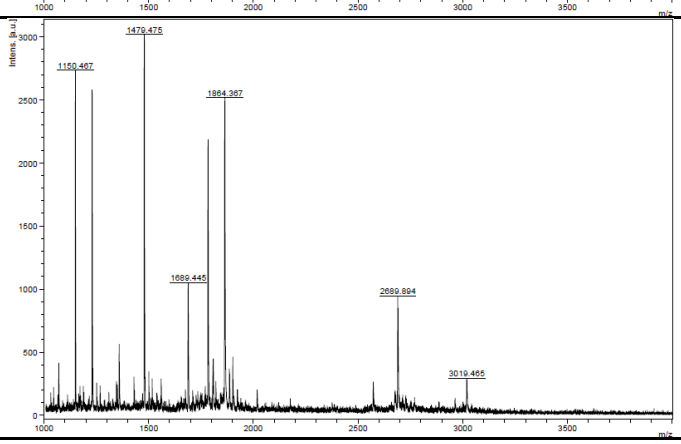
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.2
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.5
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.3

CPG-oligonucleotide + 3.7% HCl

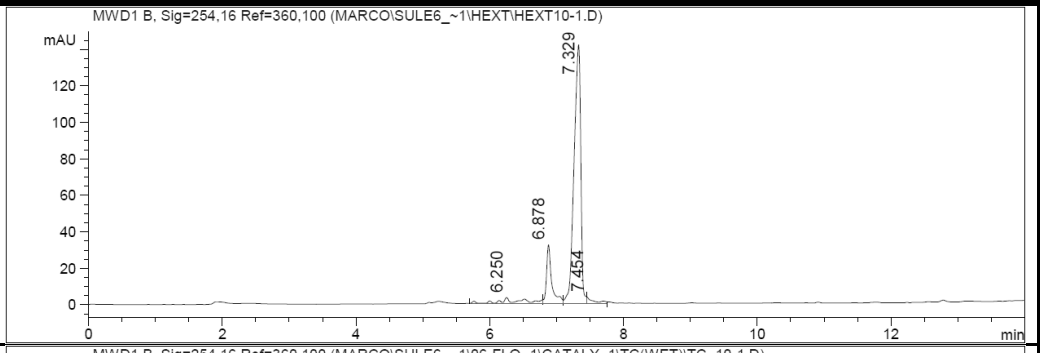
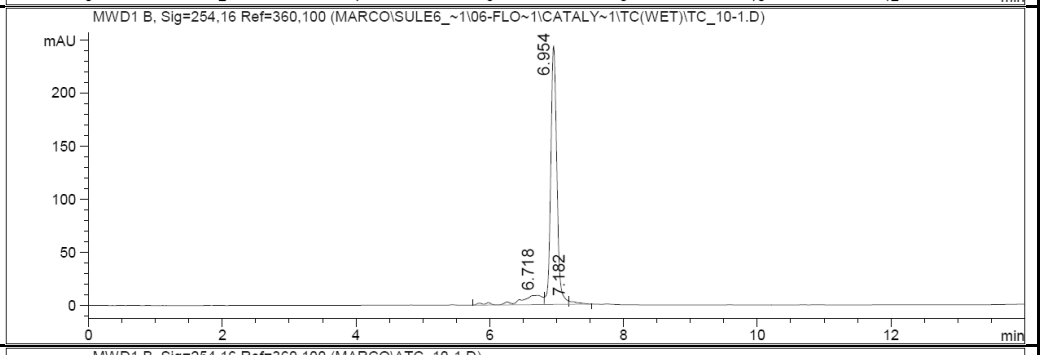
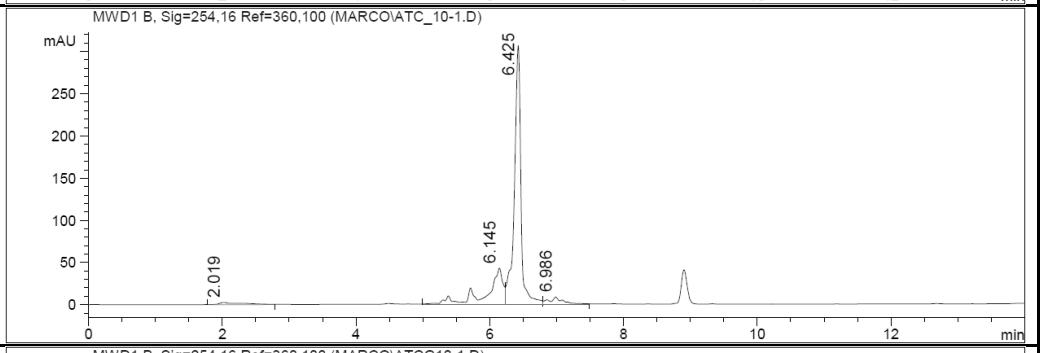
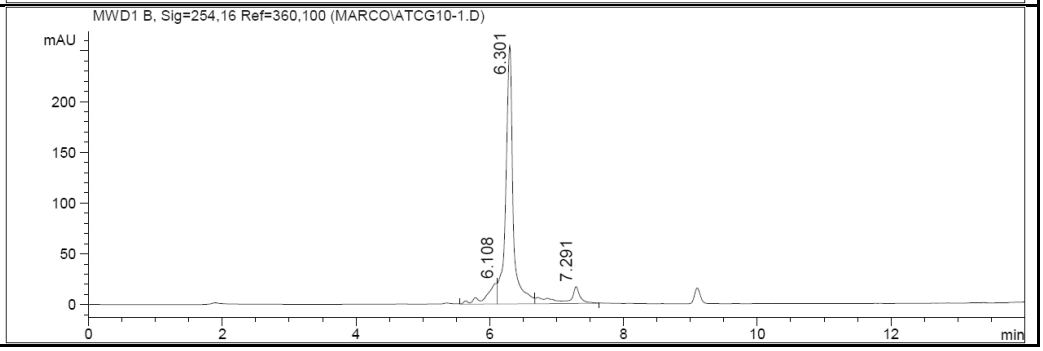
According to the representative procedure (RP-05) solid support coupled oligonucleotide (20 nmol) was treated with 3.7% HCl.

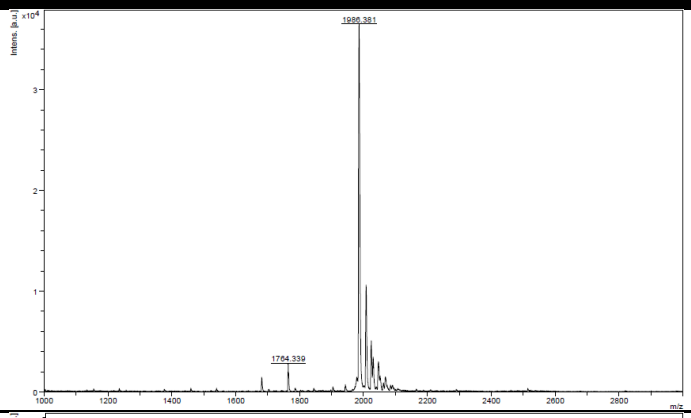
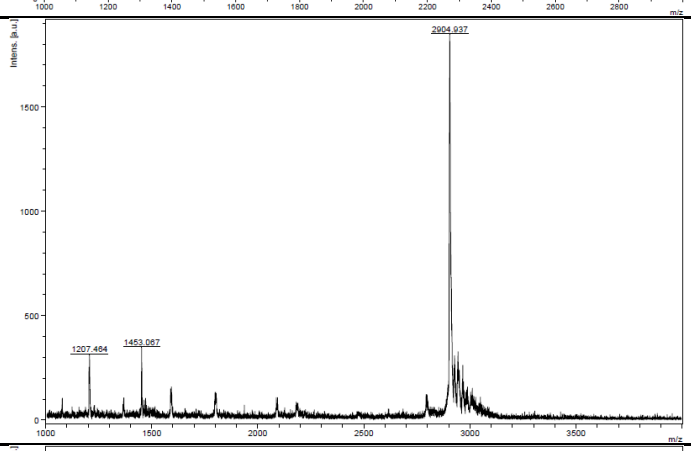
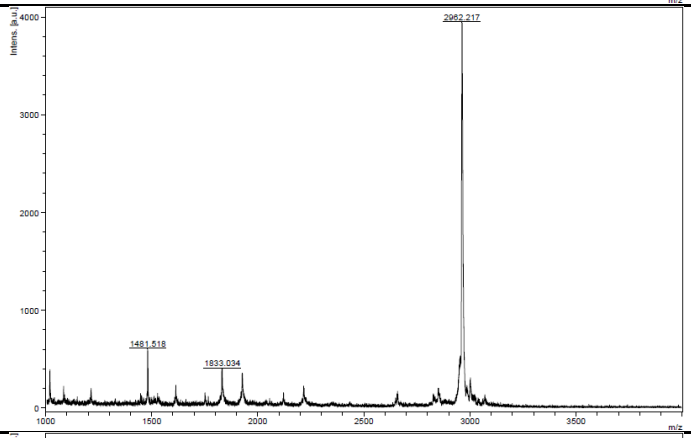
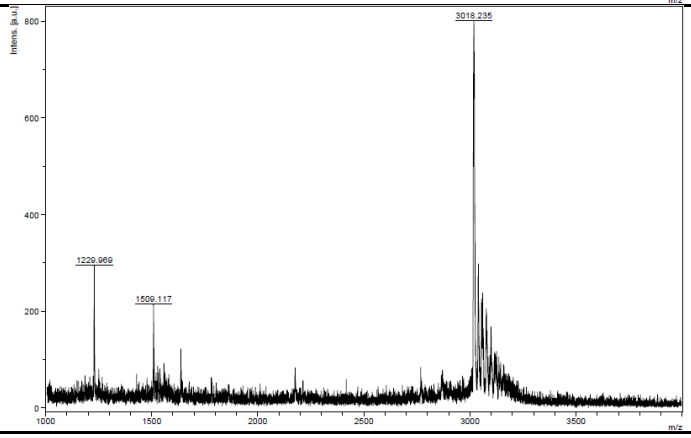
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.5
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = n.d.
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.5

CPG-oligonucleotide + AgOAc

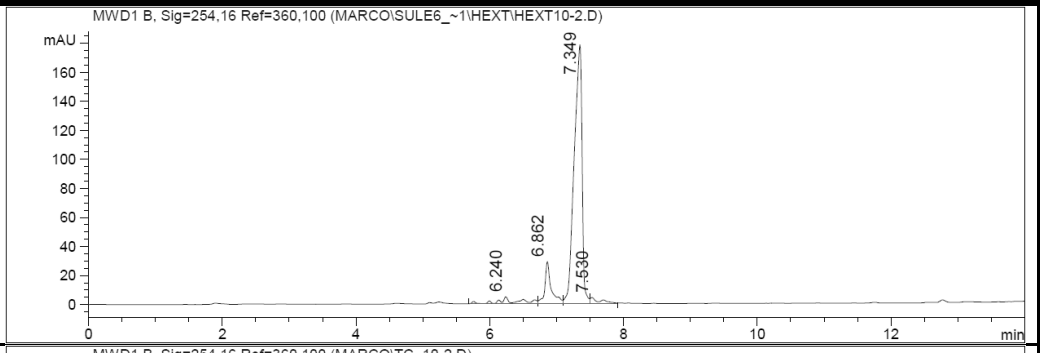
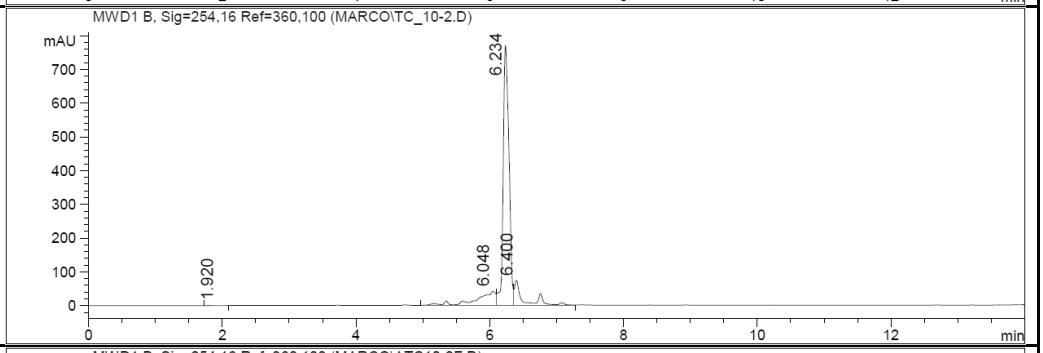
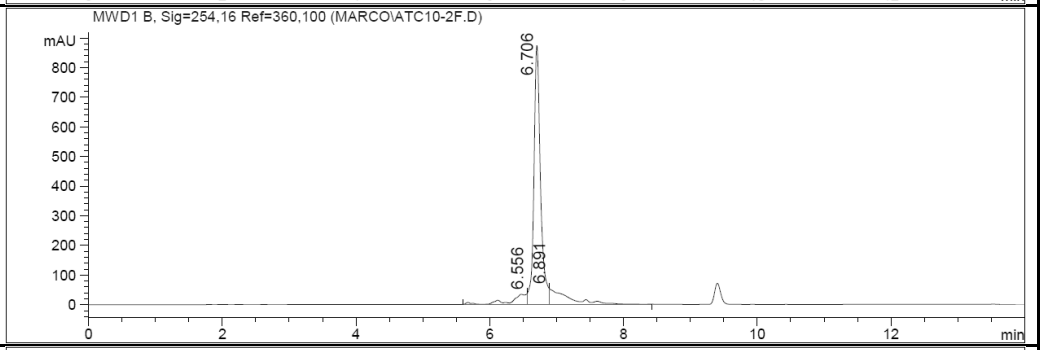
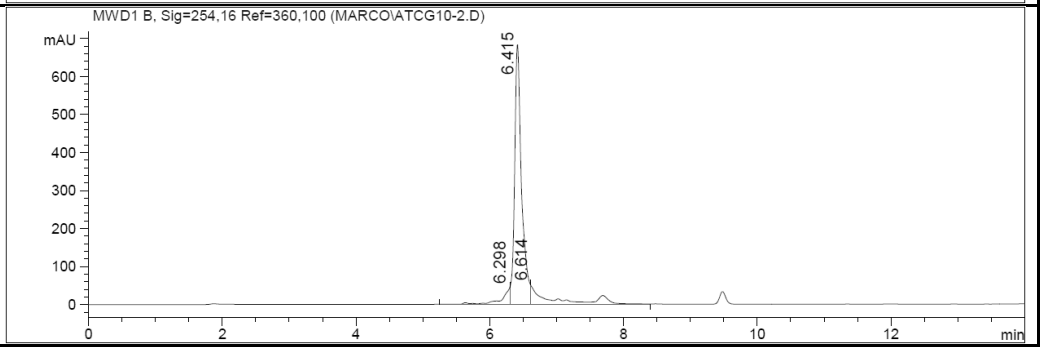
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with AgOAc (200 equiv., 4 µmol) in dry CH_2Cl_2.

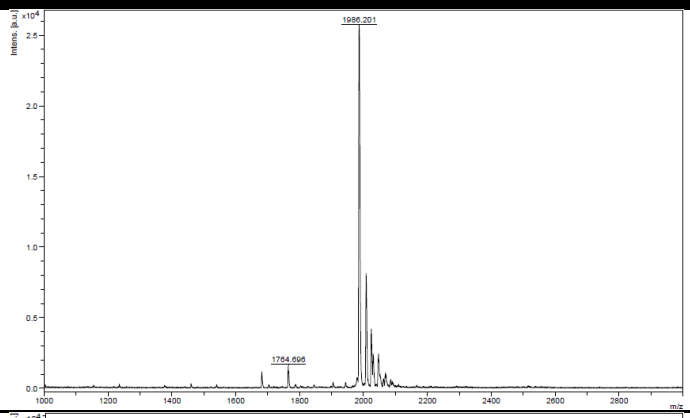
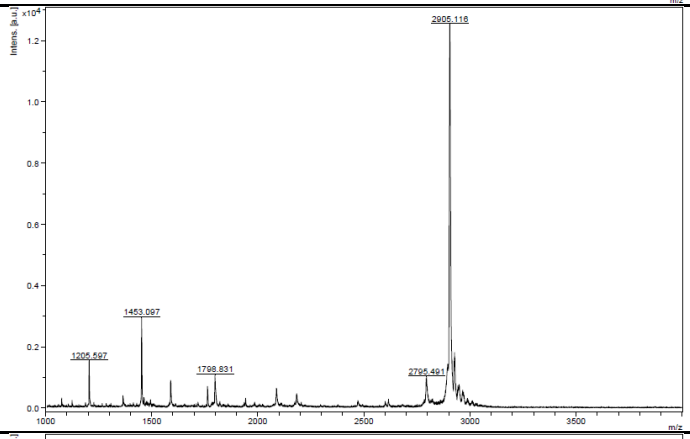
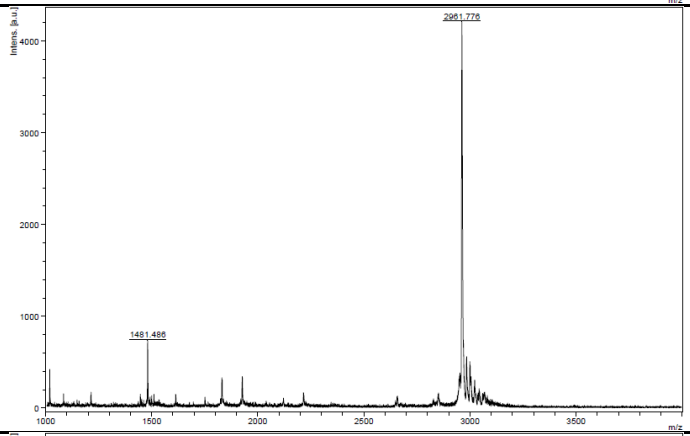
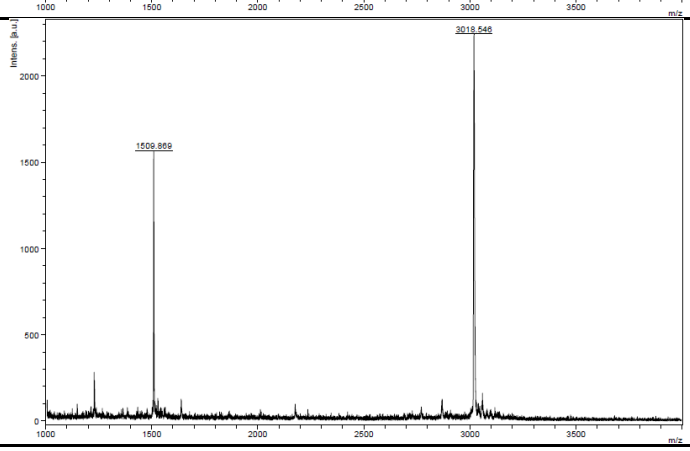
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.4
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.2
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.2

CPG-oligonucleotide + AgOTf

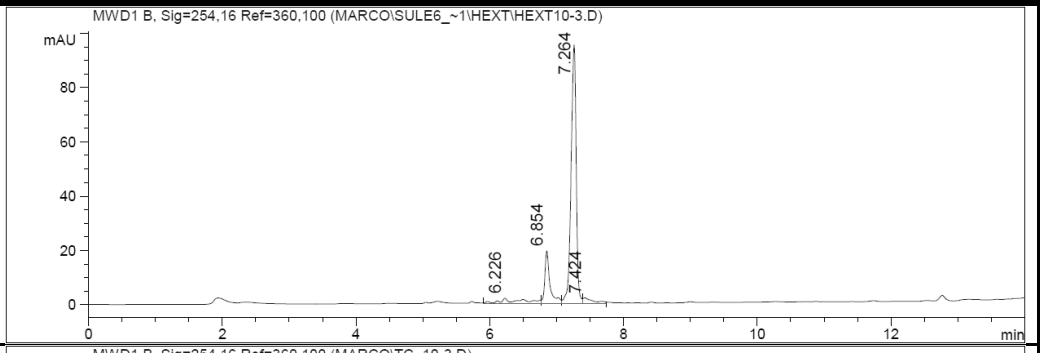
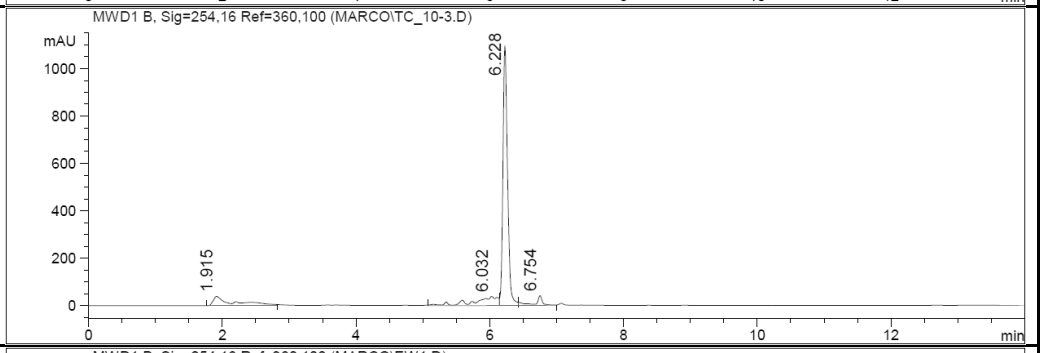
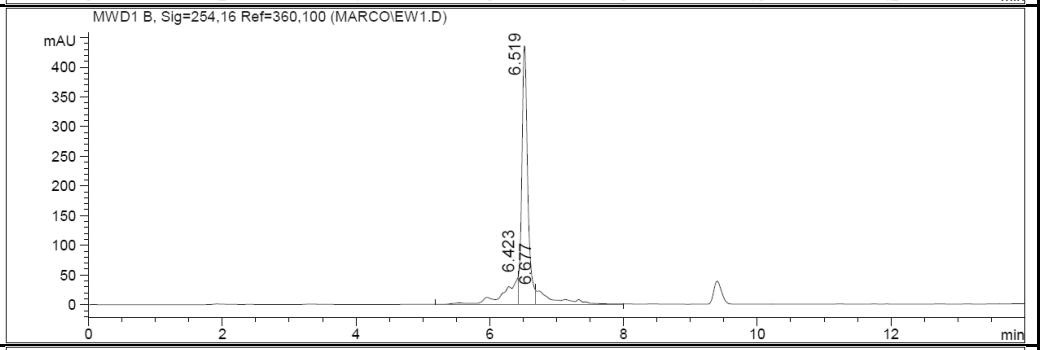
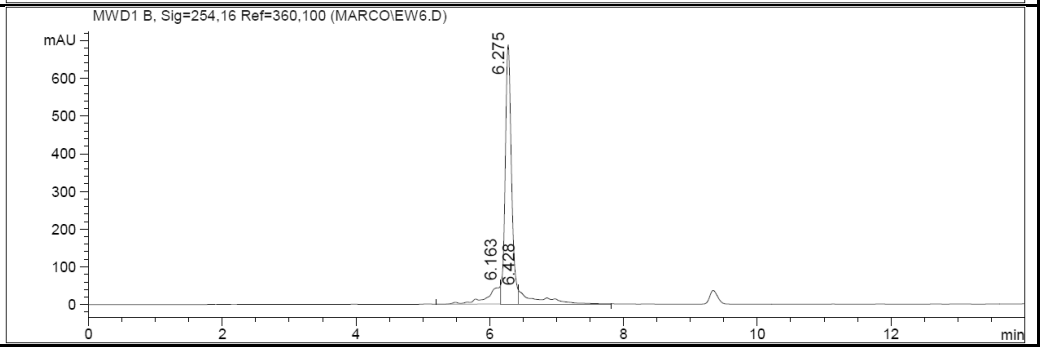
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with AgOTf (200 equiv., 4 µmol) in dry ACN.

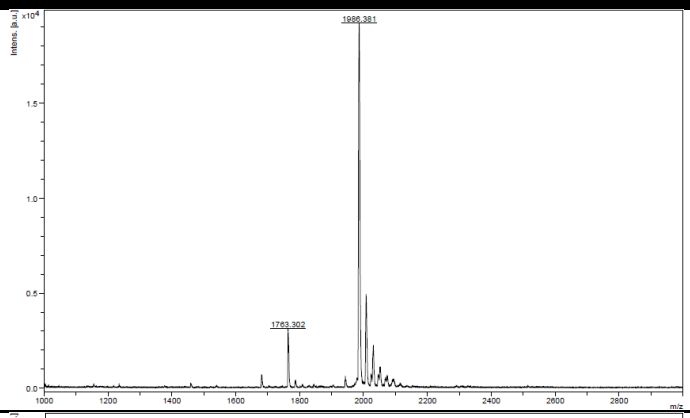
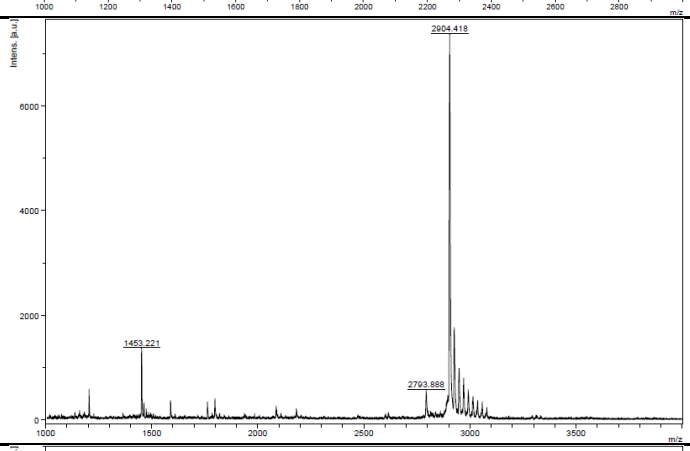
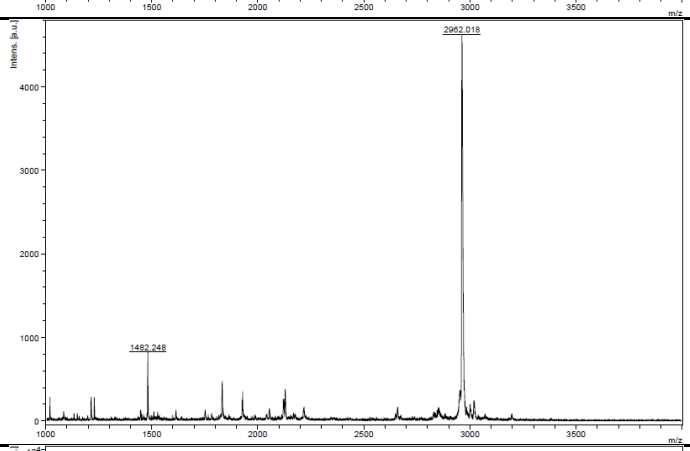
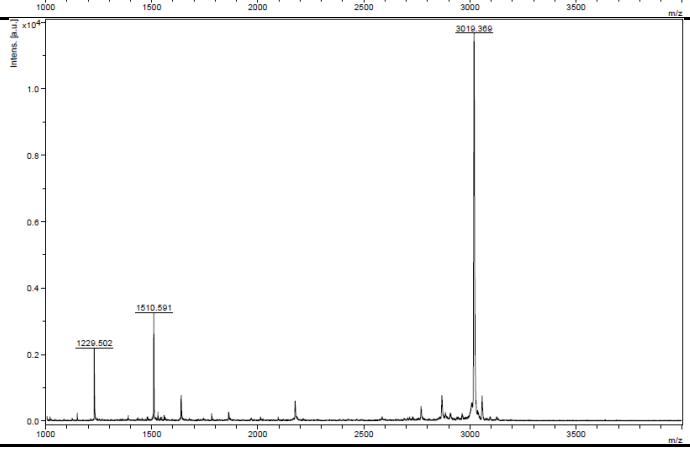
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.1
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

CPG-oligonucleotide + $AgSbF_6$

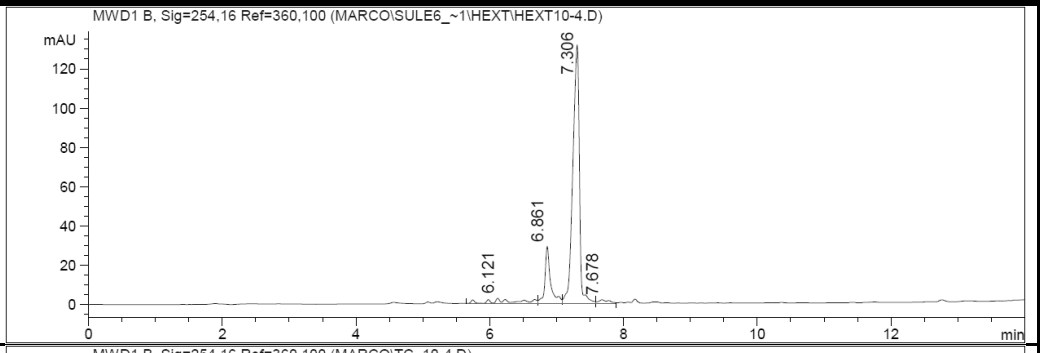
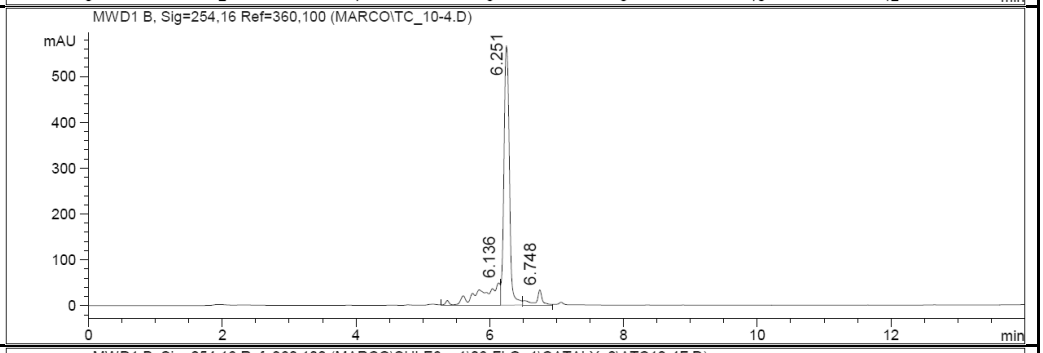
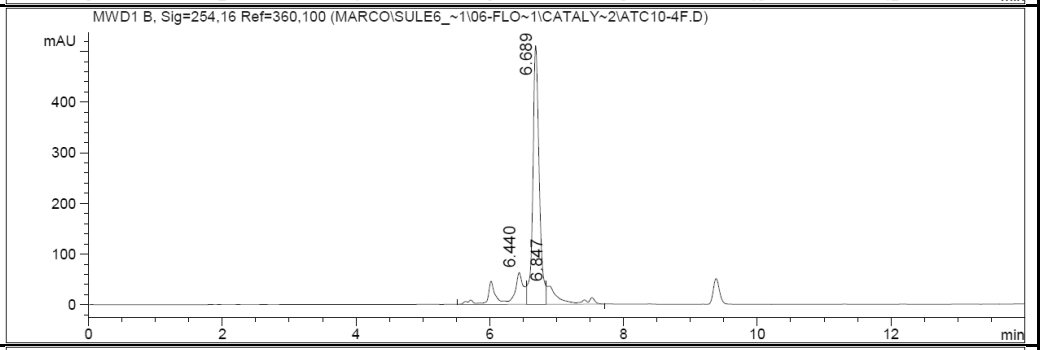
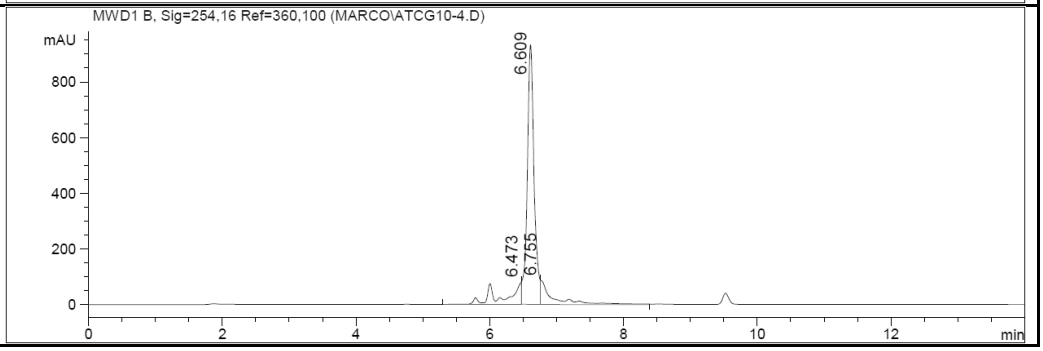
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $AgSbF_6$ (200 equiv., 4 µmol) in dry ACN.

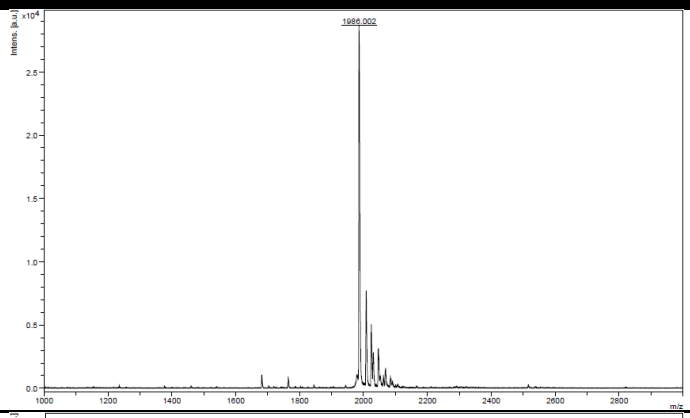
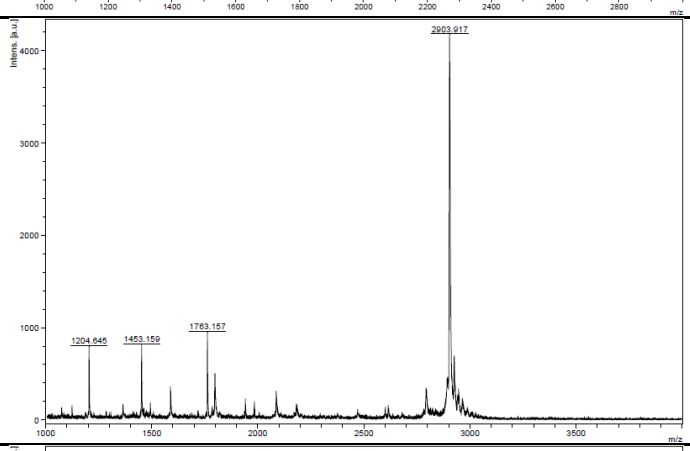
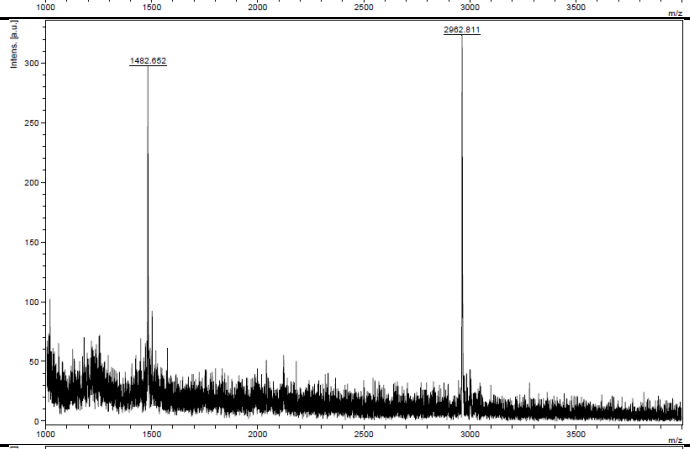
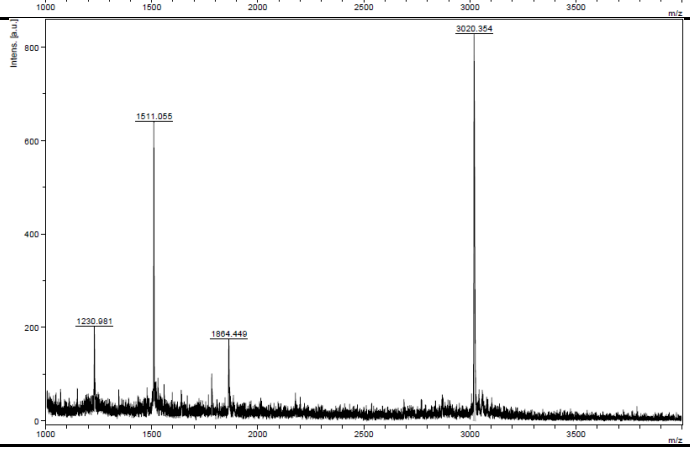
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.4
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.4

CPG-oligonucleotide + $BiBr_3$

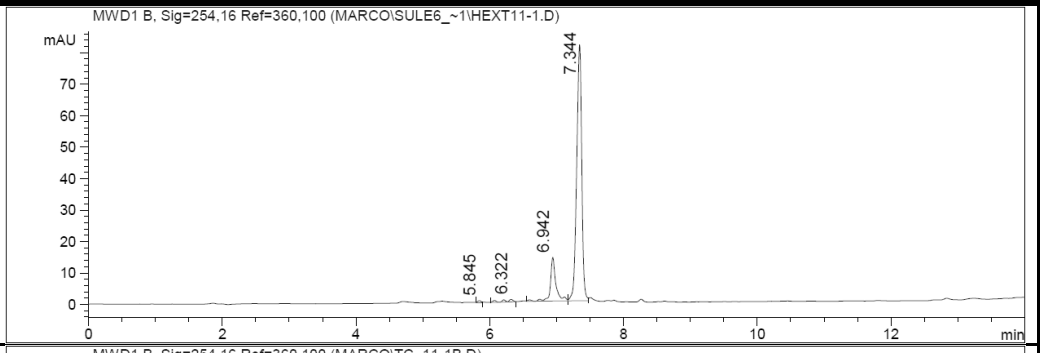
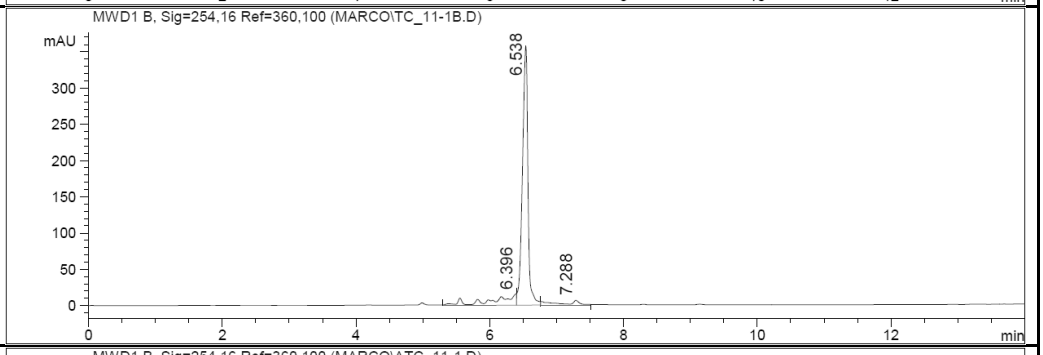
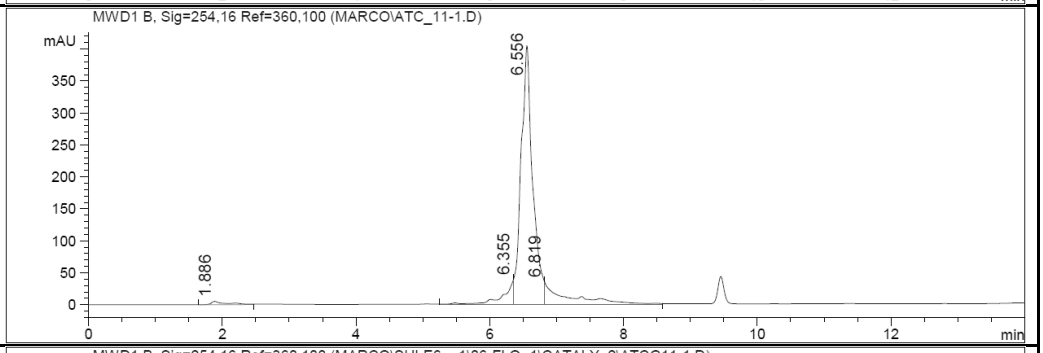
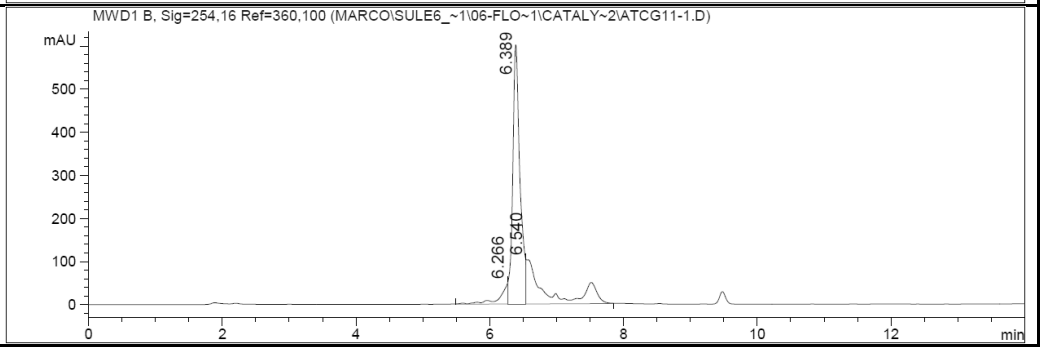
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $BiBr_3$ (200 equiv., 4 µmol) in dry ACN.

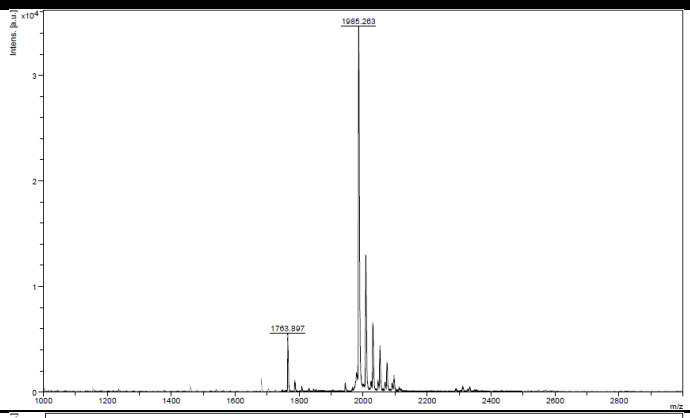
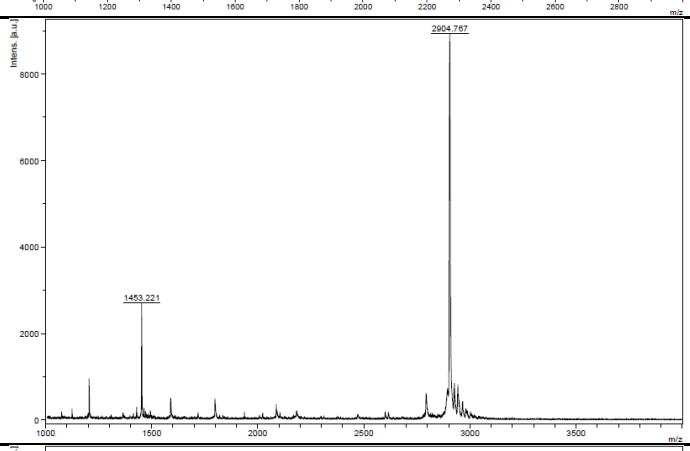
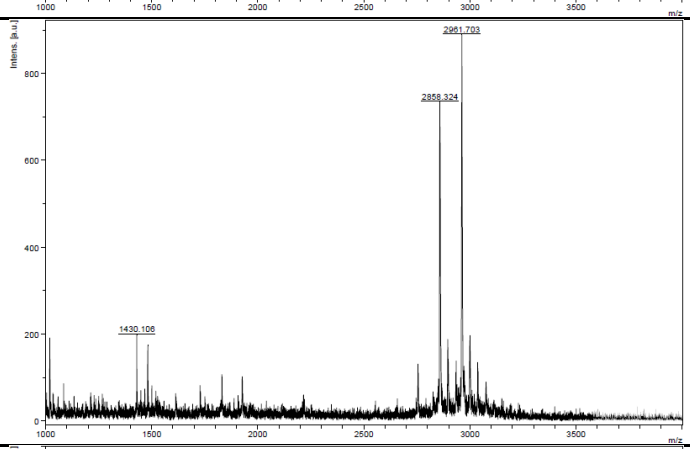
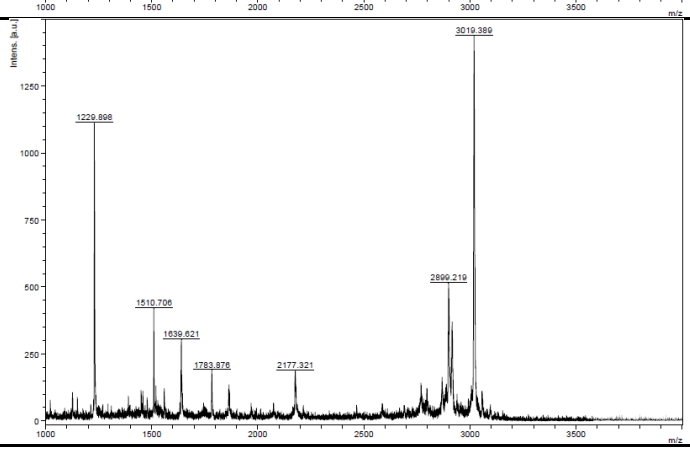
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2903.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3020.4

CPG-oligonucleotide + $Bi(OTf)_3$

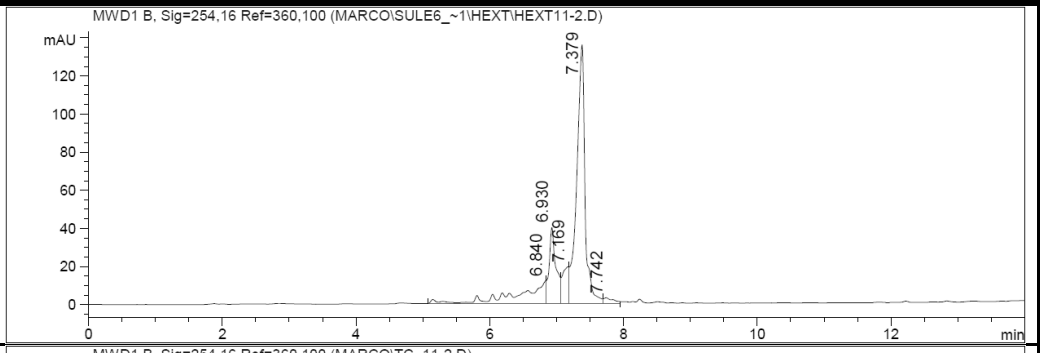
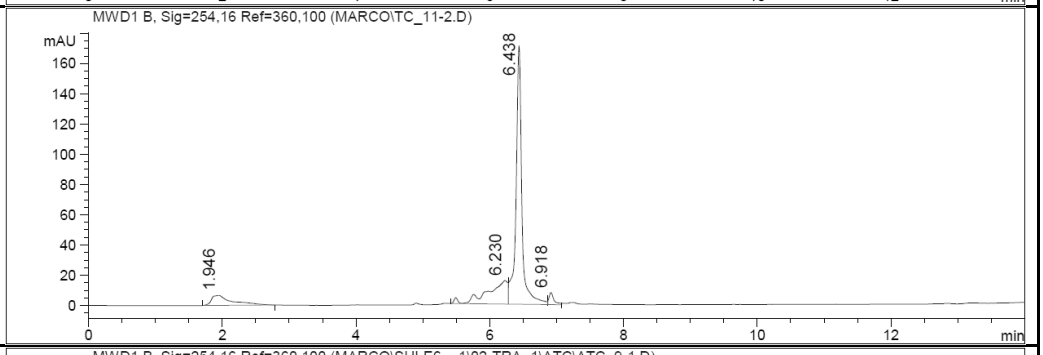
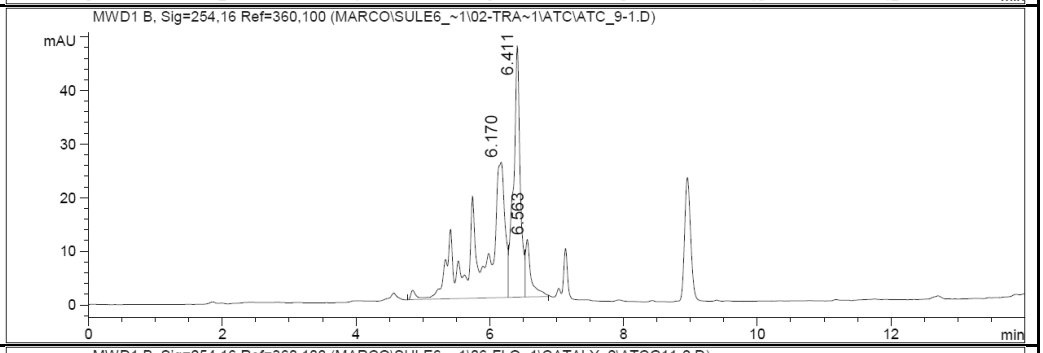
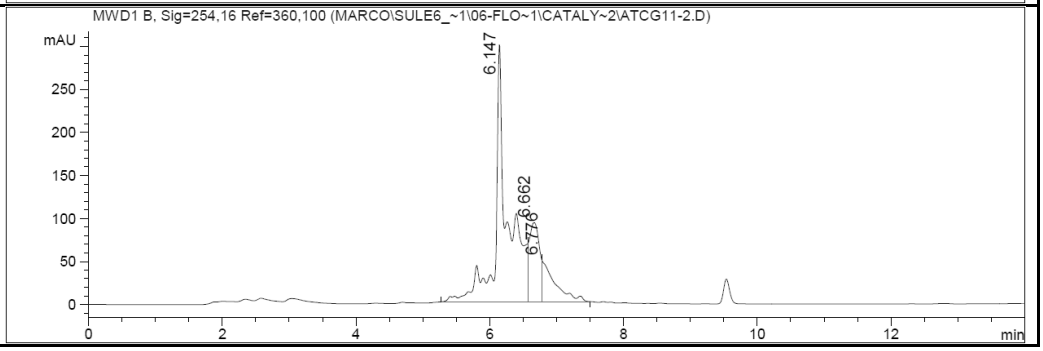
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Bi(OTf)_3$ (200 equiv., 4 µmol) in dry MeOH.

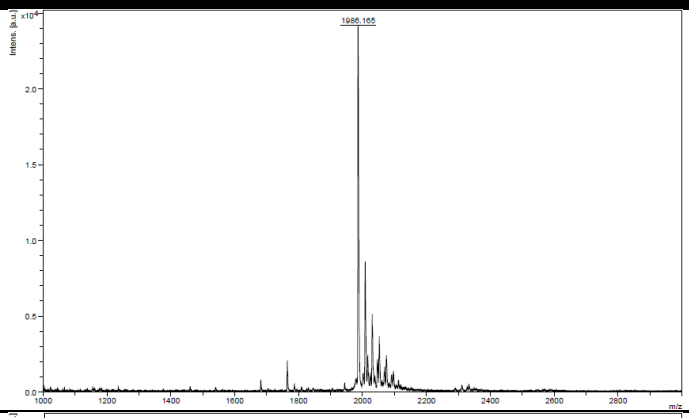
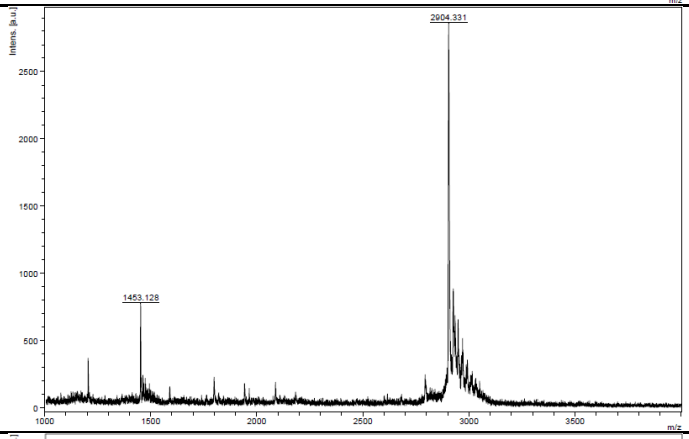
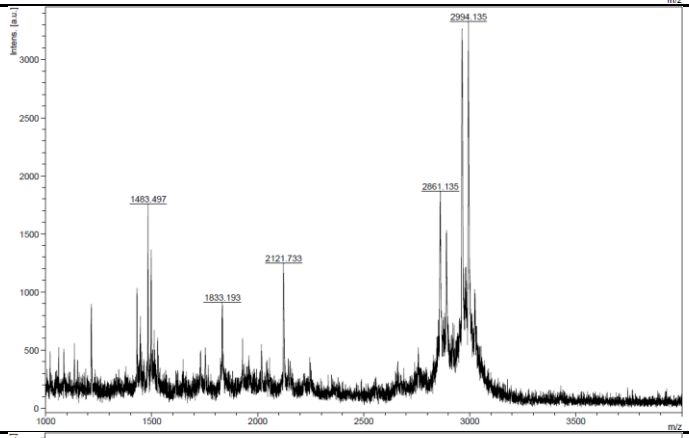
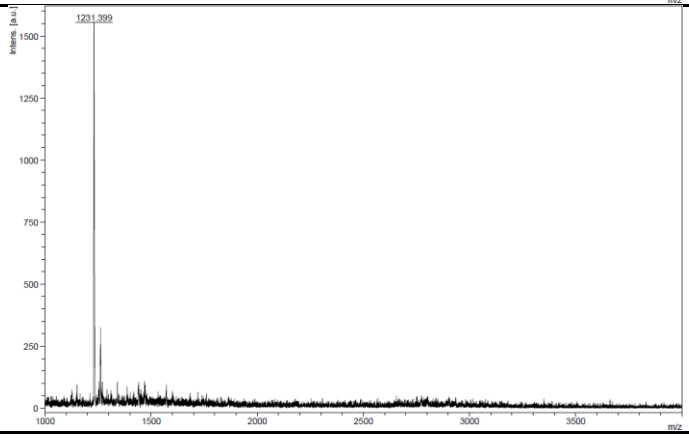
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.8
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.7
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.4

CPG-oligonucleotide + $Ce(NH_4)_2(NO_3)_6$

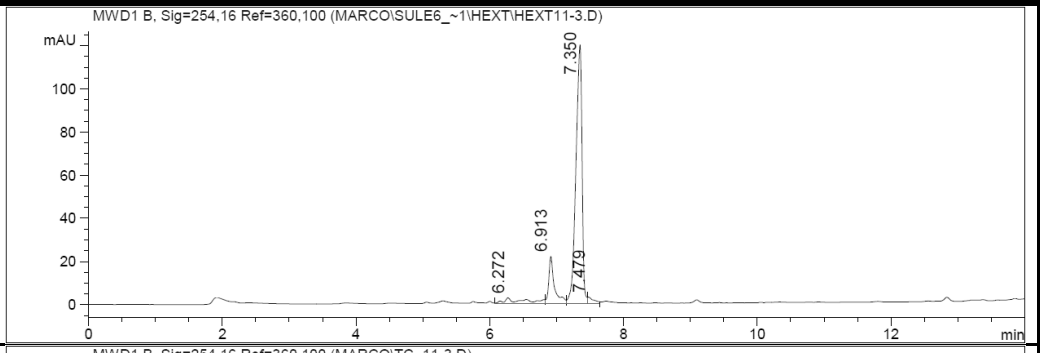
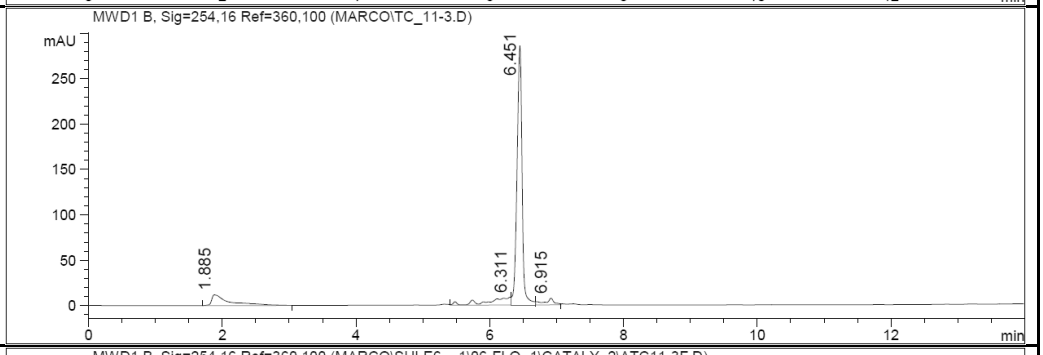
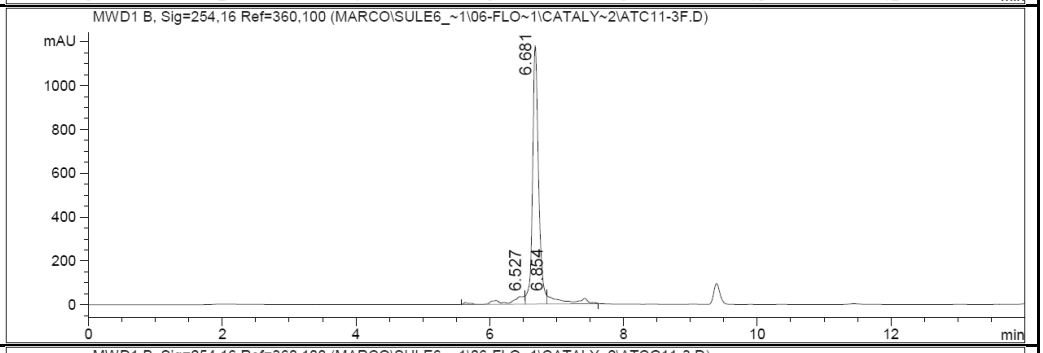
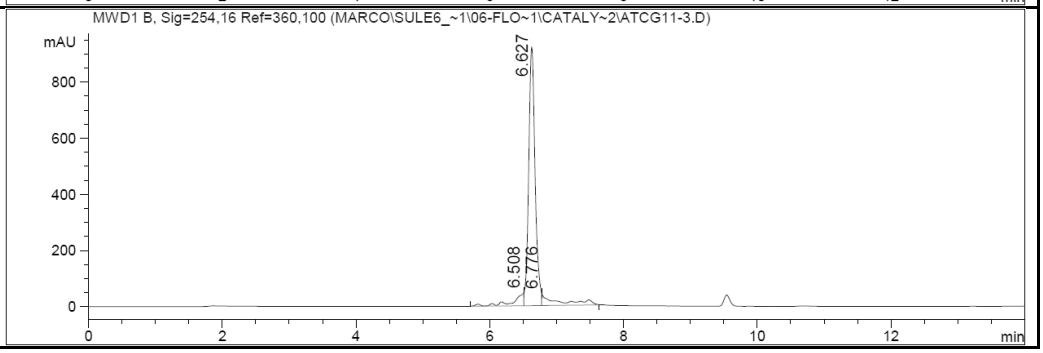
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Ce(NH_4)_2(NO_3)_6$ (200 equiv., 4 µmol) in dry MeOH.

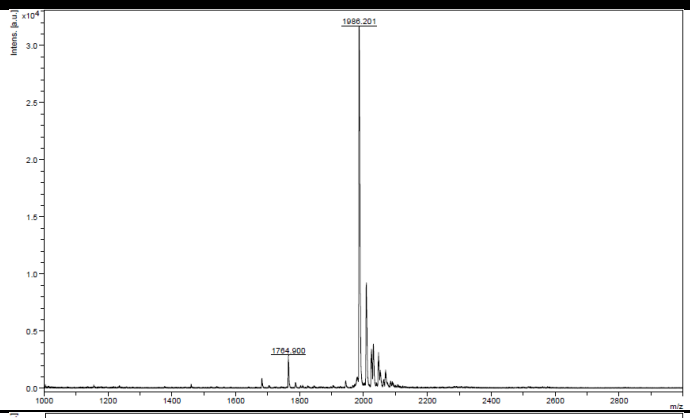
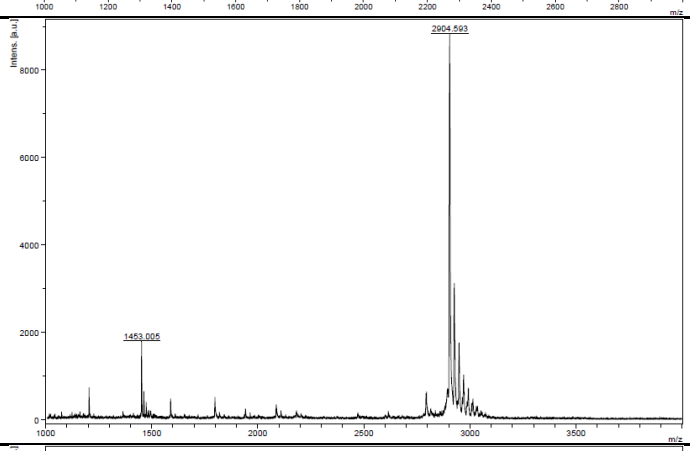
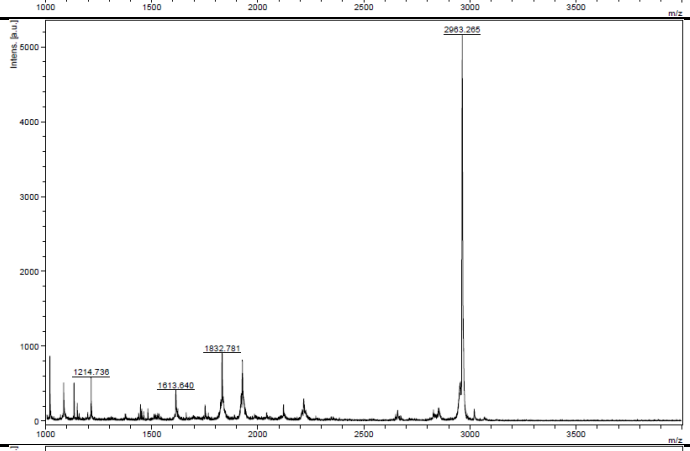
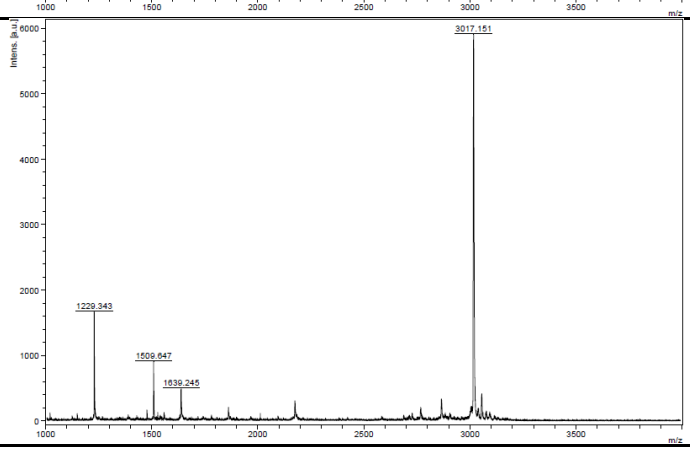
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.3
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.2
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = n.d.

CPG-oligonucleotide + $Co(acac)_3$

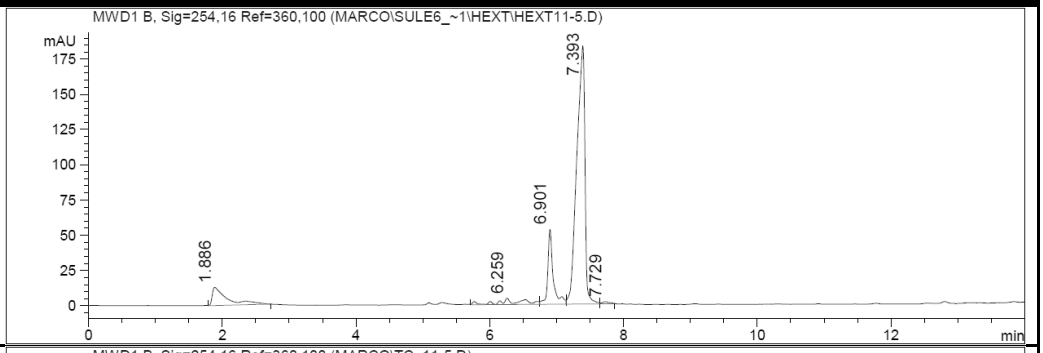
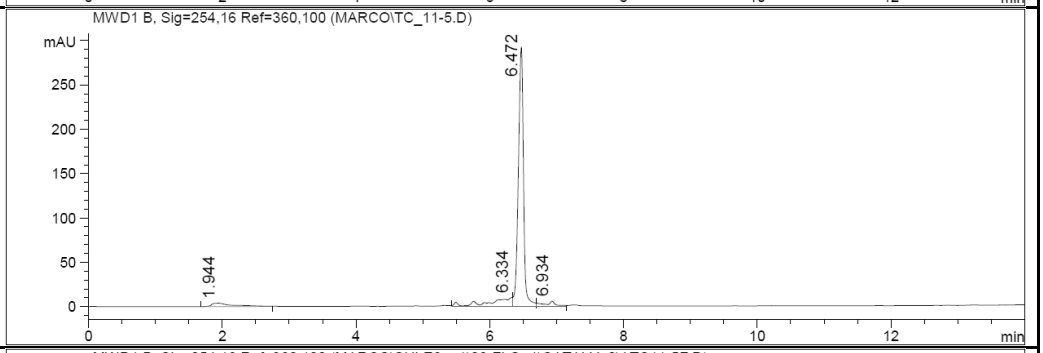
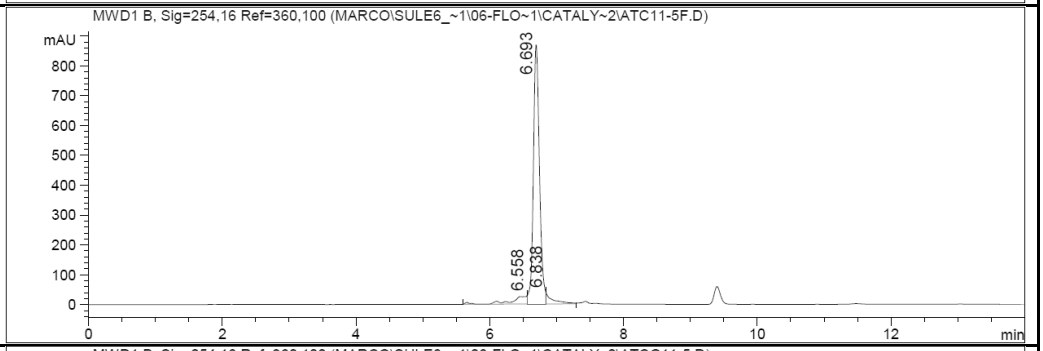
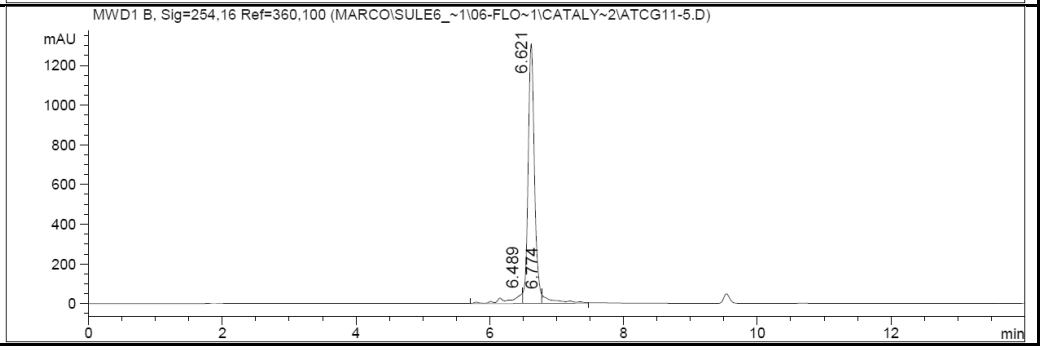
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Co(acac)_3$ (200 equiv., 4 µmol) in dry ACN.

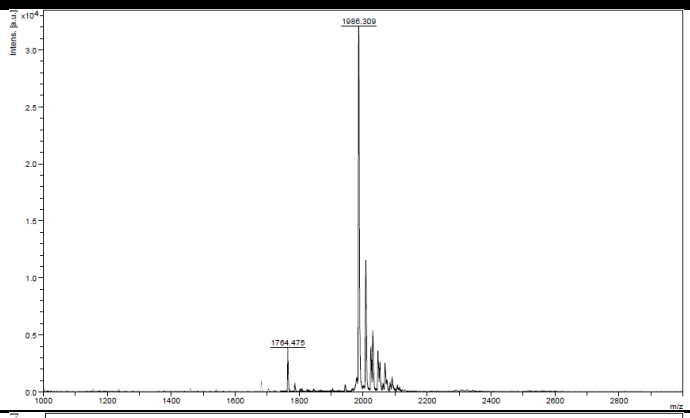
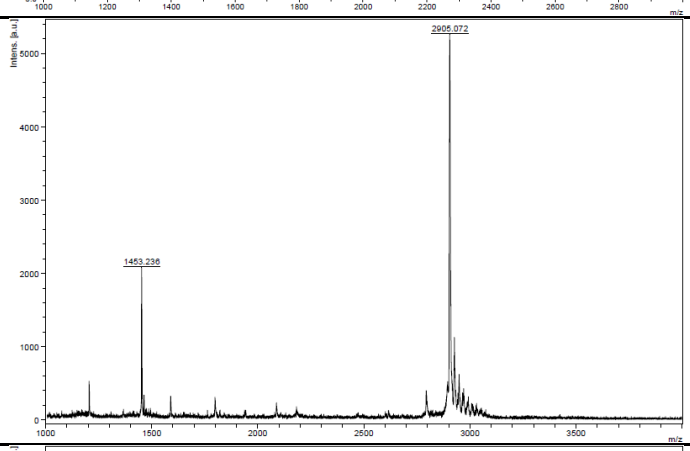
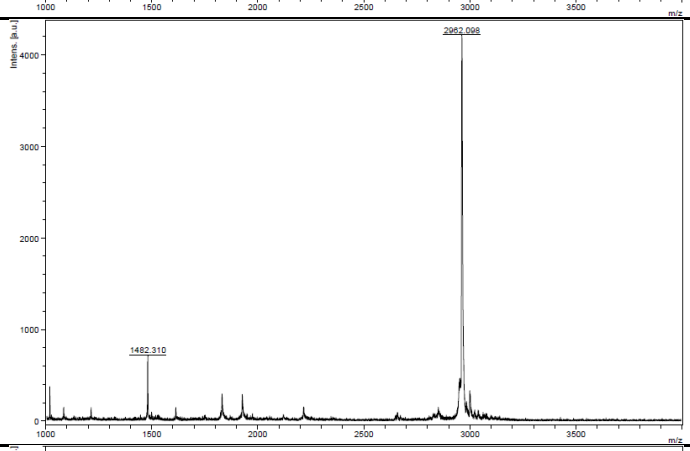
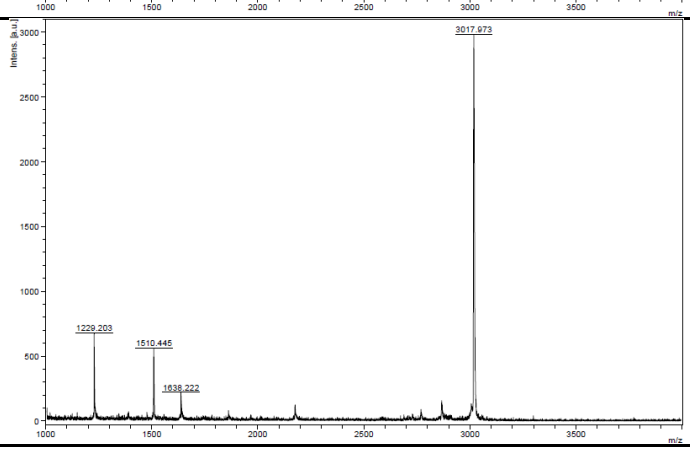
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.6
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.2

CPG-oligonucleotide + CuCl

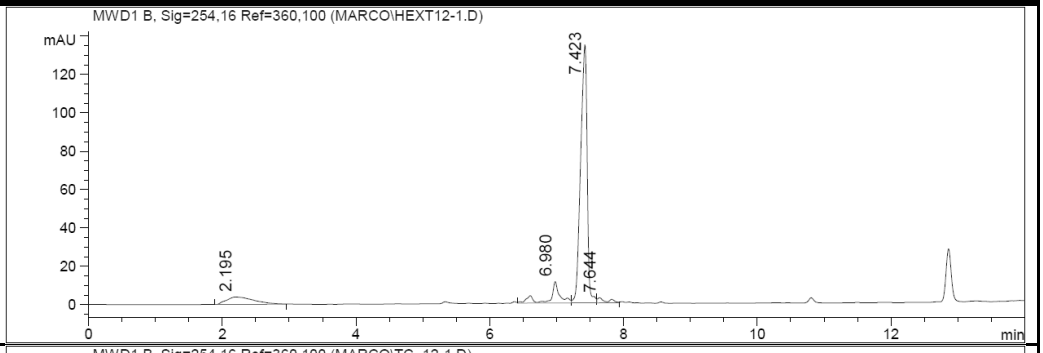
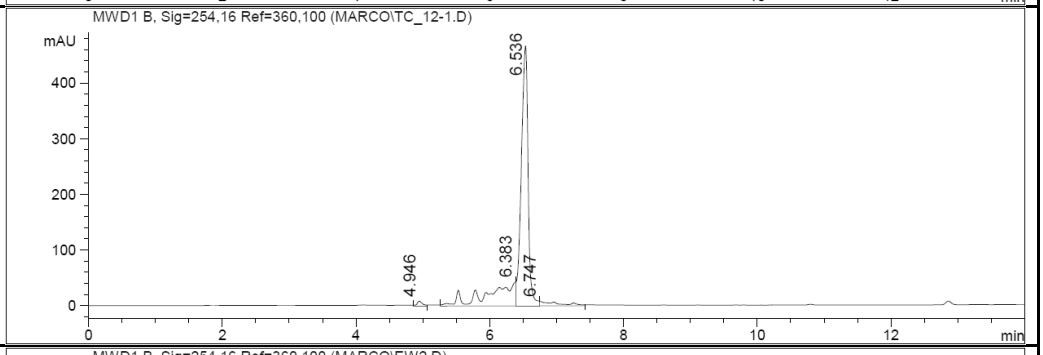
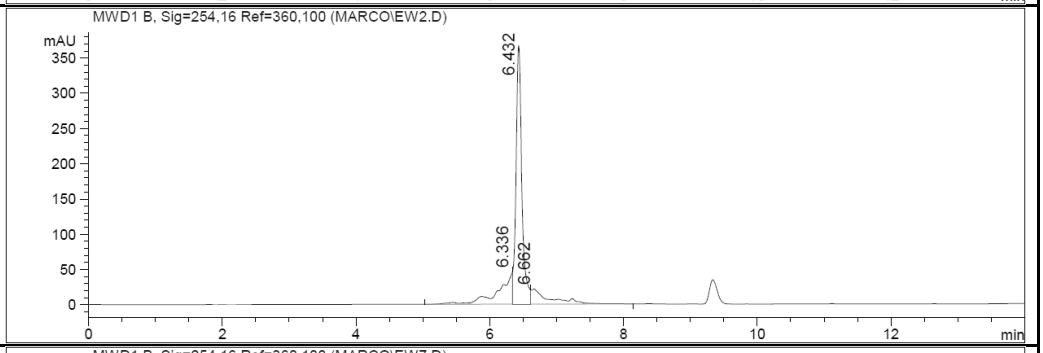
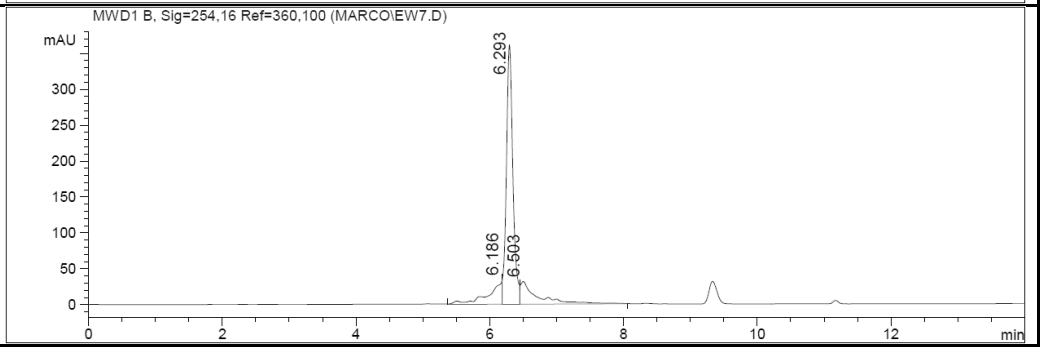
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with CuCl (200 equiv., 4 µmol) in dry MeOH.

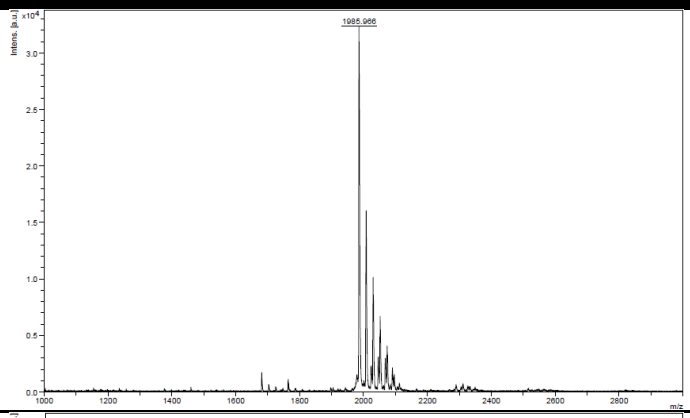
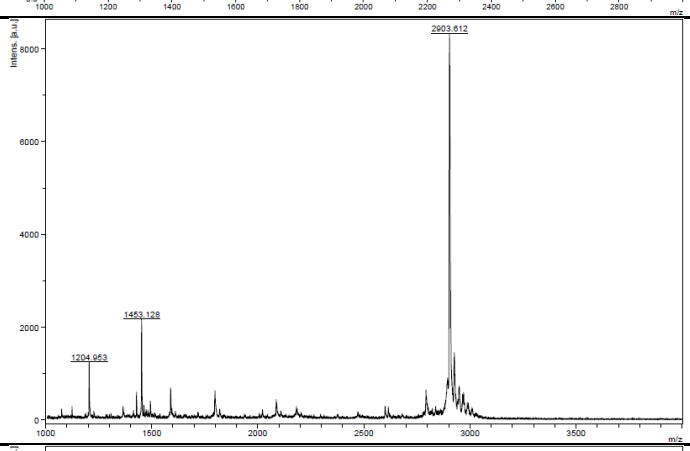
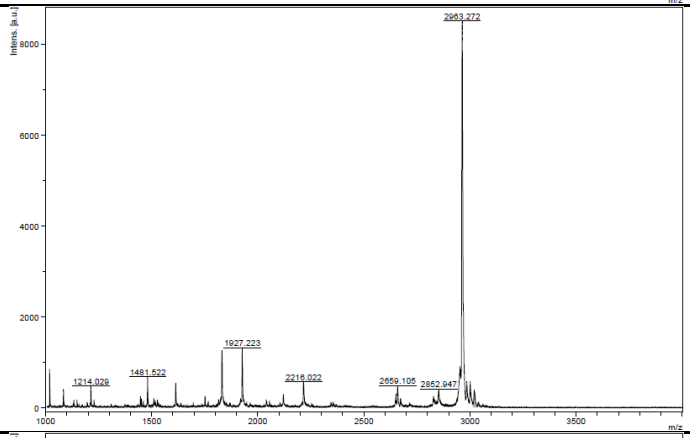
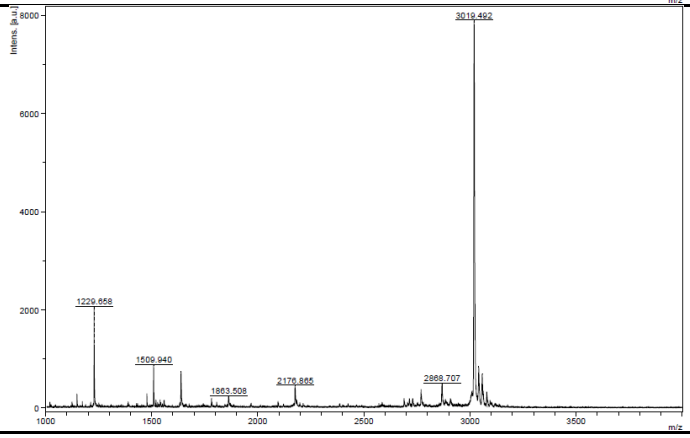
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.1
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.1
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.0

CPG-oligonucleotide + $Cu(MeCN)_4PF_6$

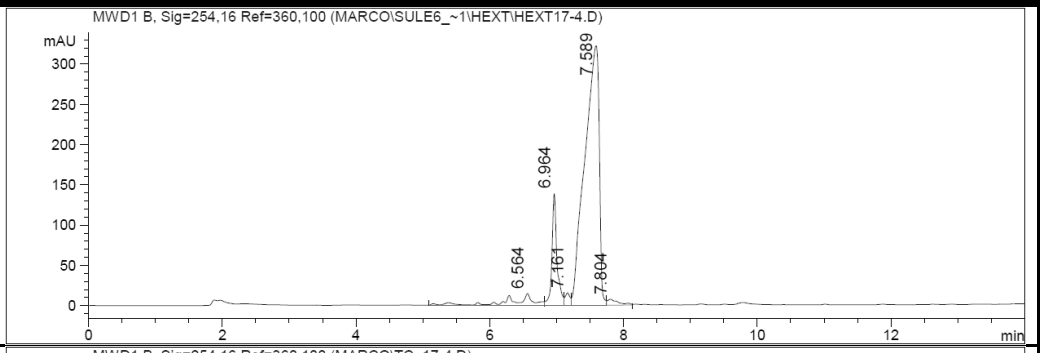
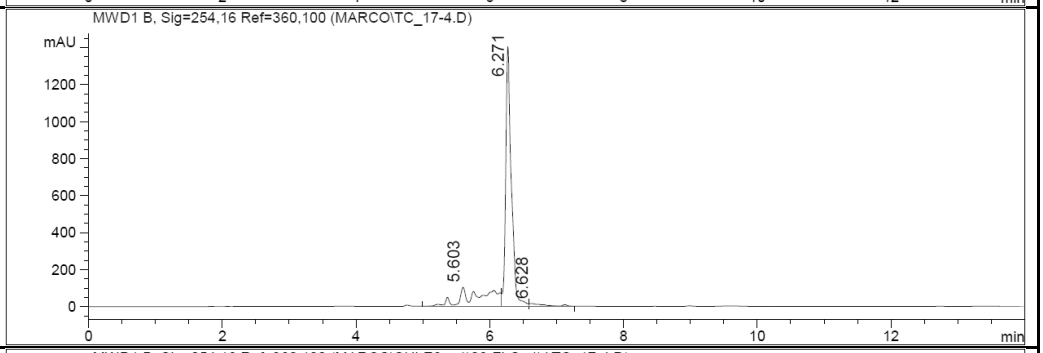
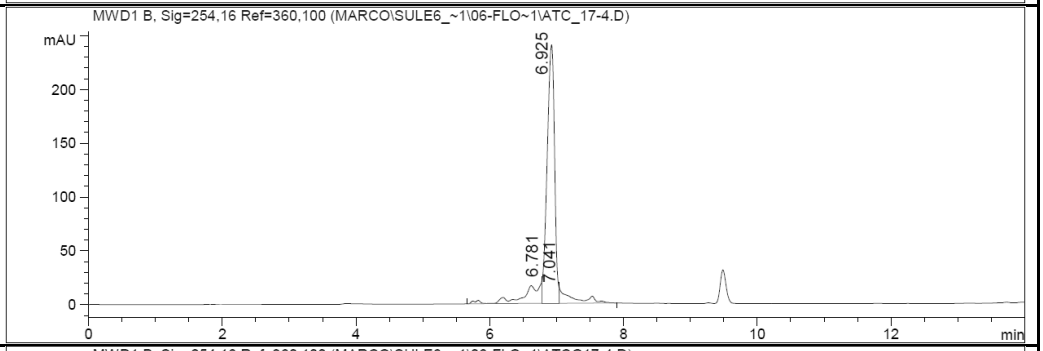
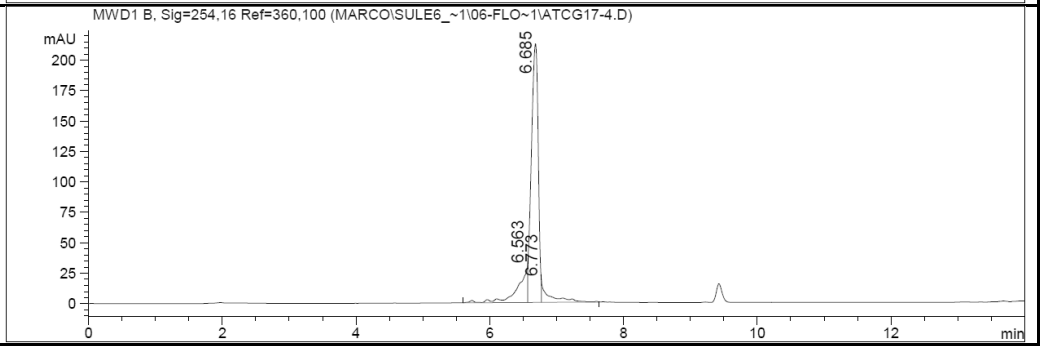
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Cu(MeCN)_4PF_6$ (200 equiv., 4 µmol) in dry ACN.

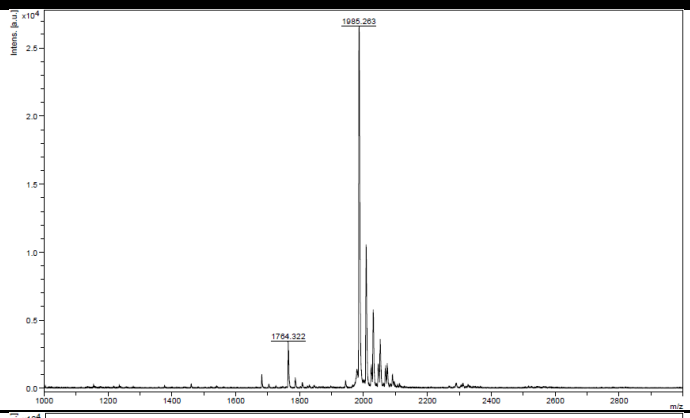
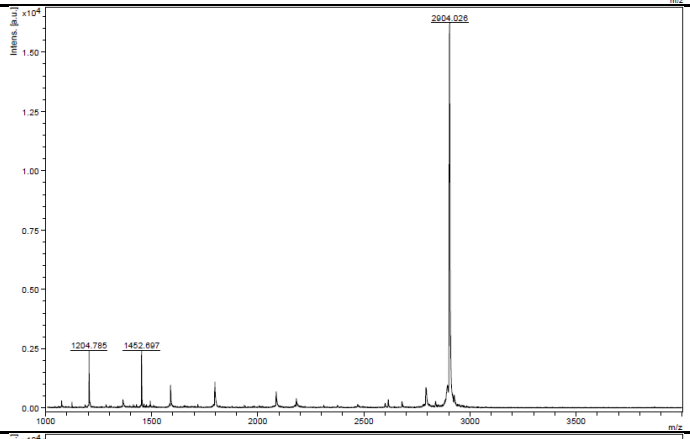
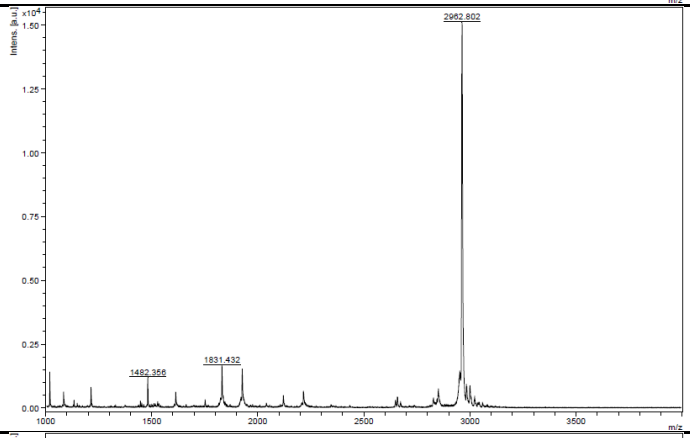
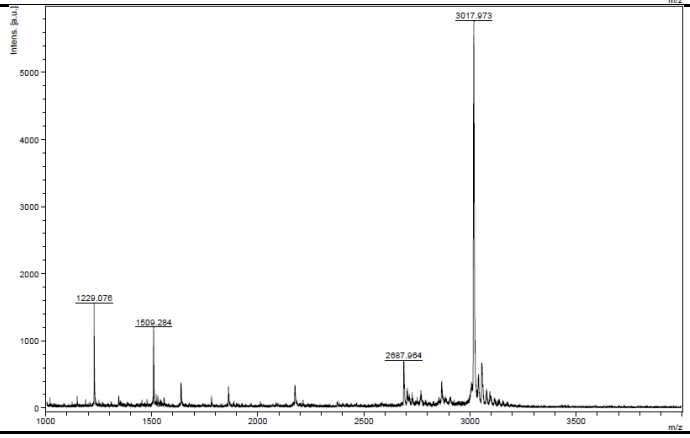
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2903.6
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.5

CPG-oligonucleotide + $Cu(OTf)_2$

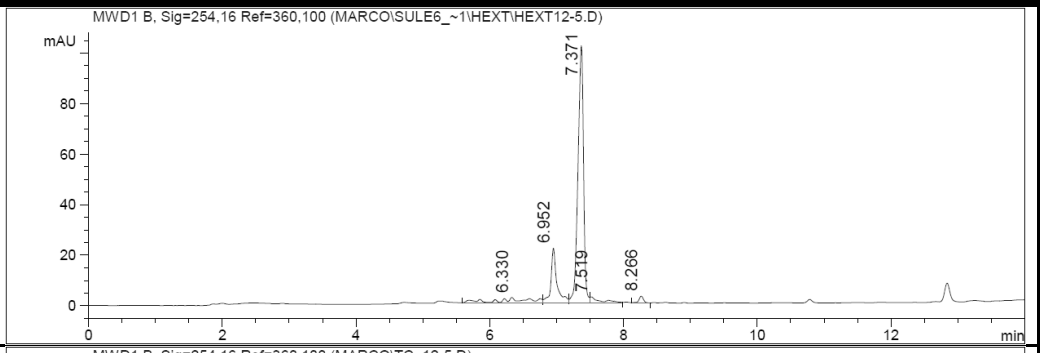
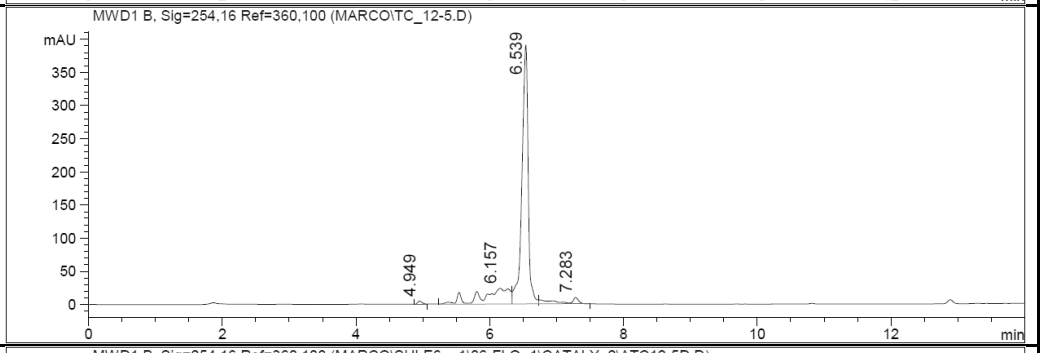
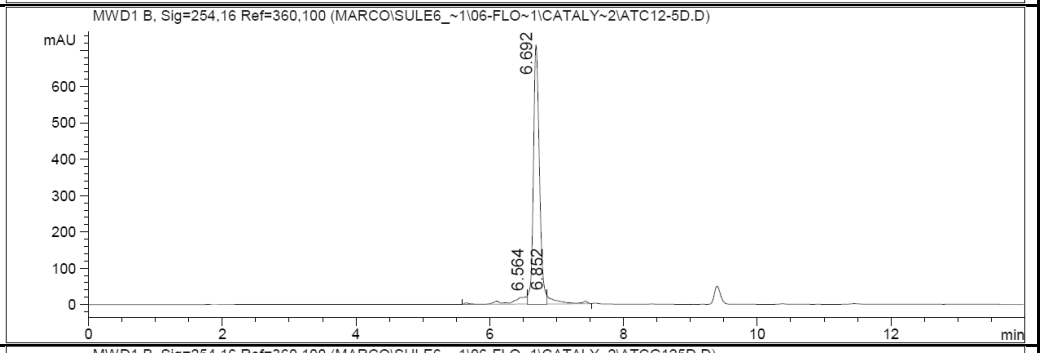
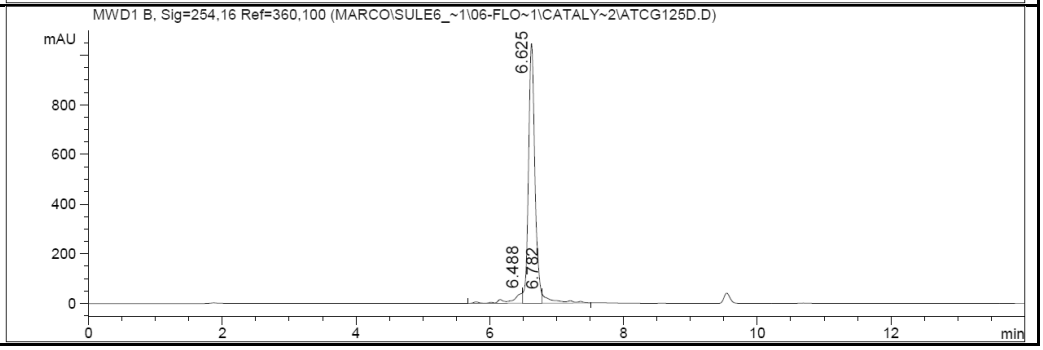
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Cu(OTf)_2$ (200 equiv., 4 µmol) in dry ACN.

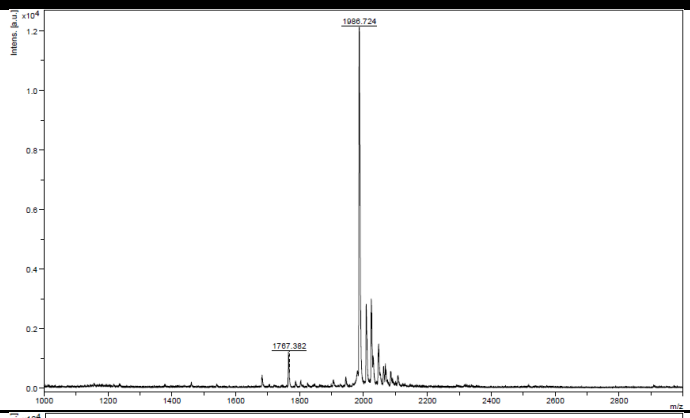
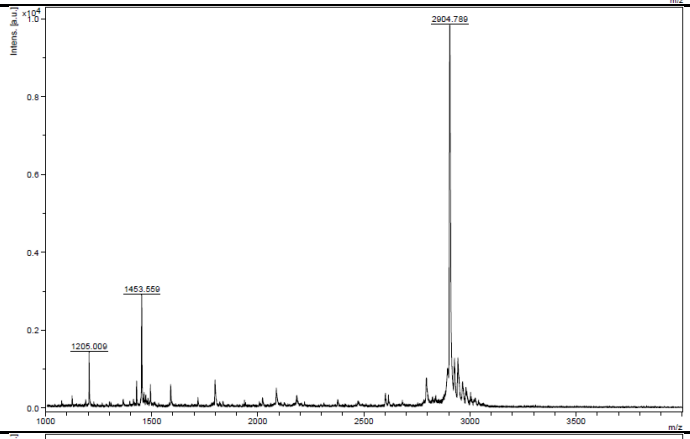
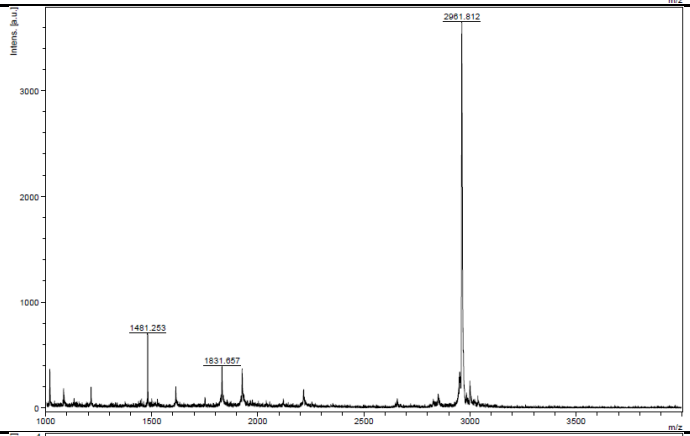
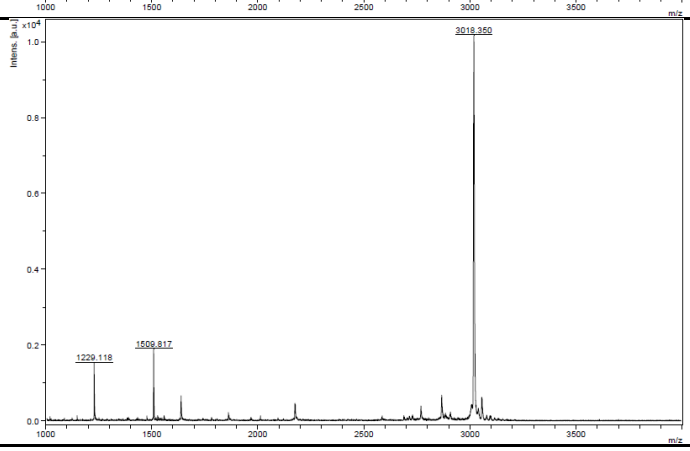
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **$AcNH-(CH_2)_6-$** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.0
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.0

CPG-oligonucleotide + $Fe(acac)_3$

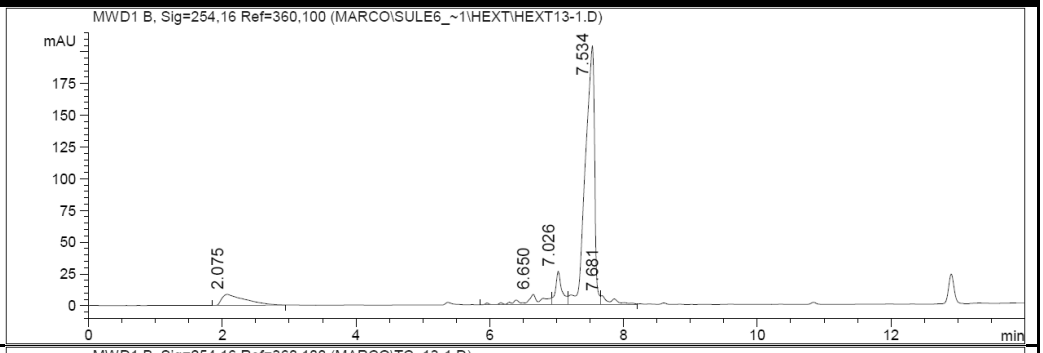
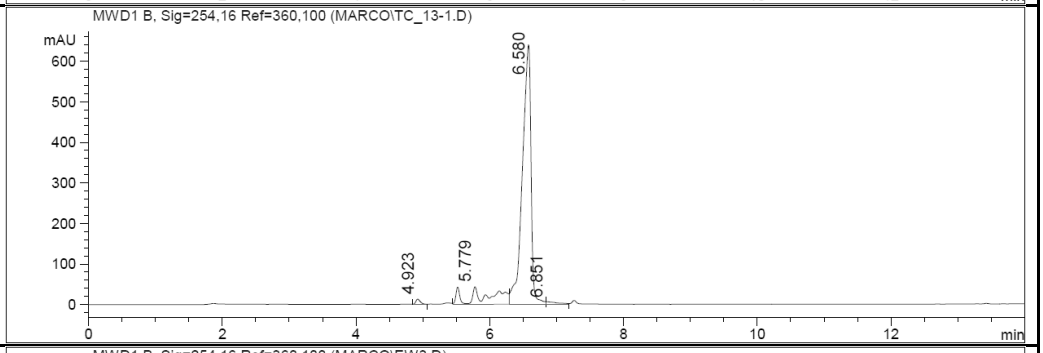
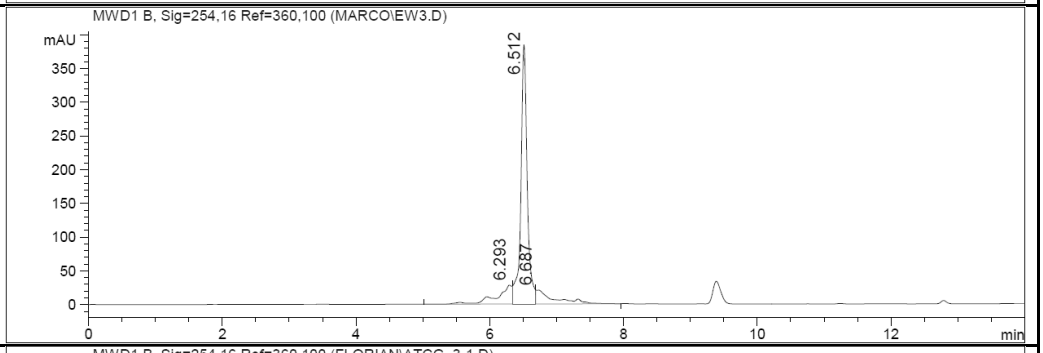
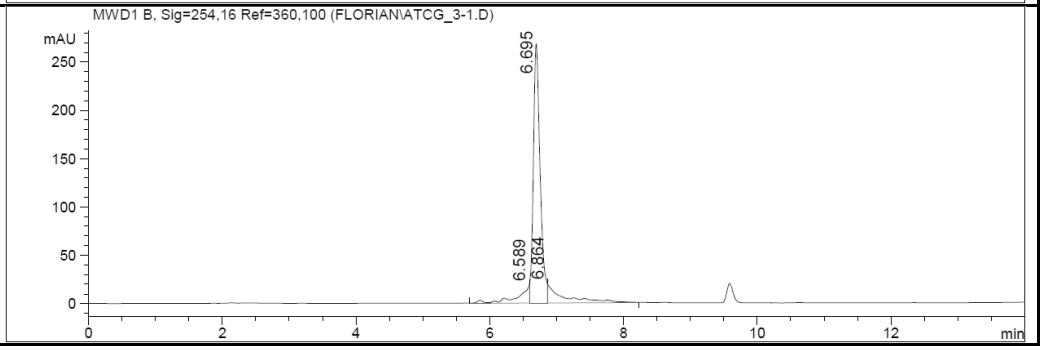
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Fe(acac)_3$ (200 equiv., 4 µmol) in dry ACN.

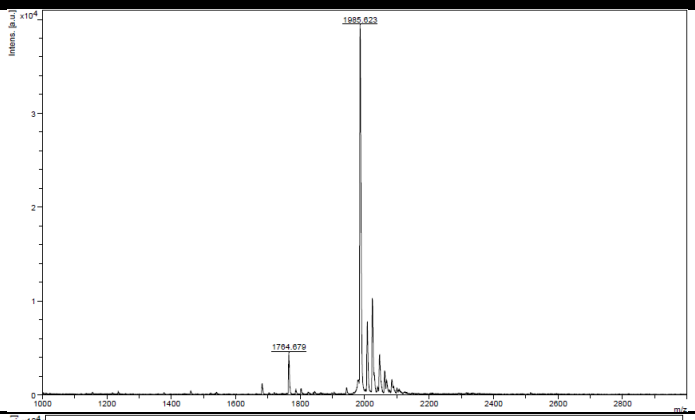
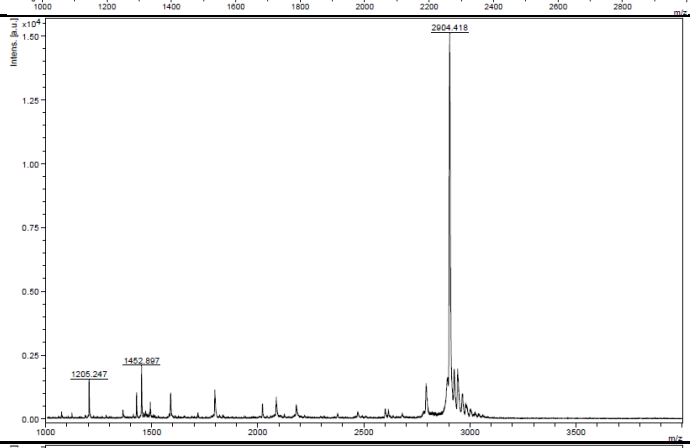
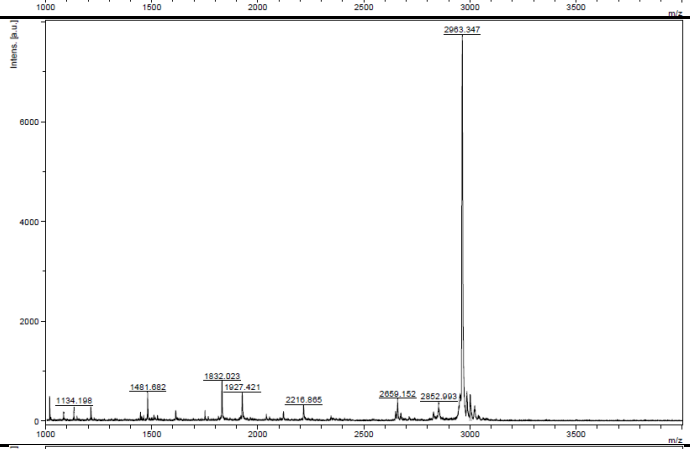
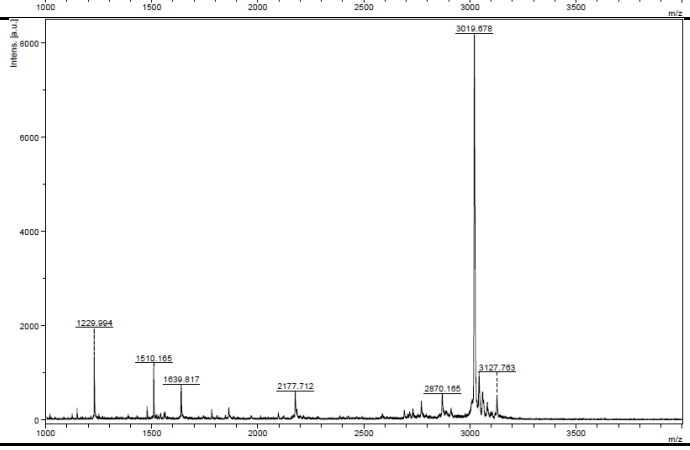
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **$AcNH-(CH_2)_6-$** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.7
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.8
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.4

CPG-oligonucleotide + $FeCl_2 \cdot 4\ H_2O$

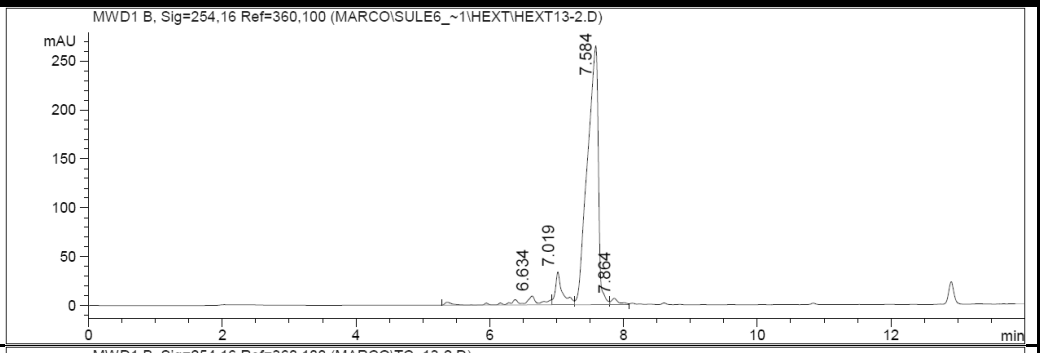
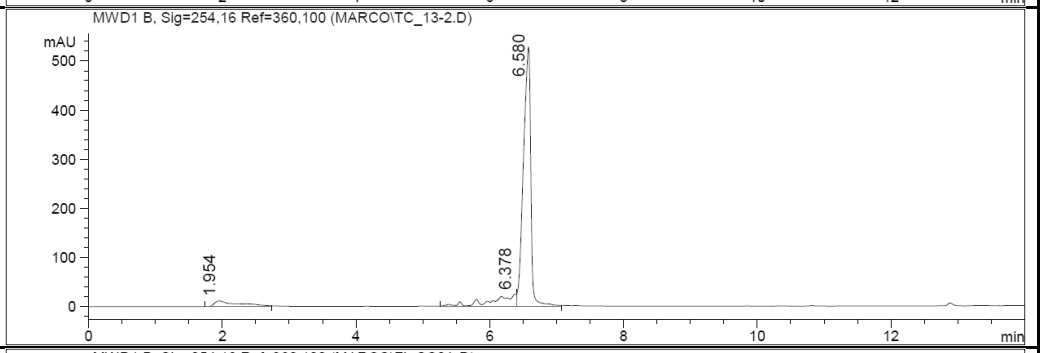
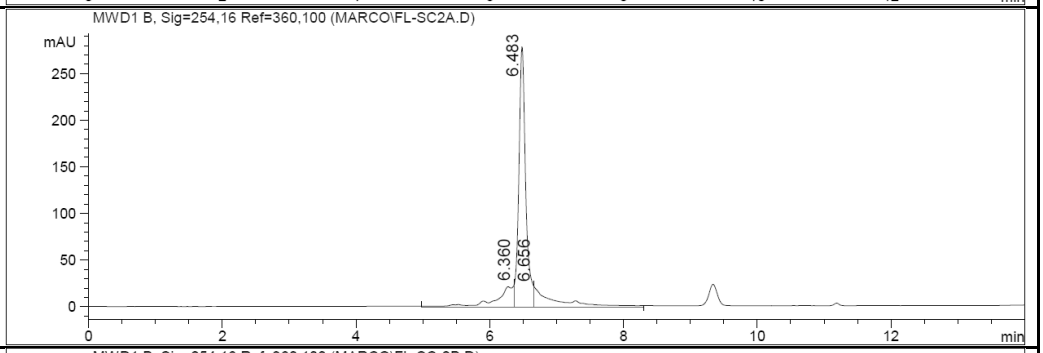
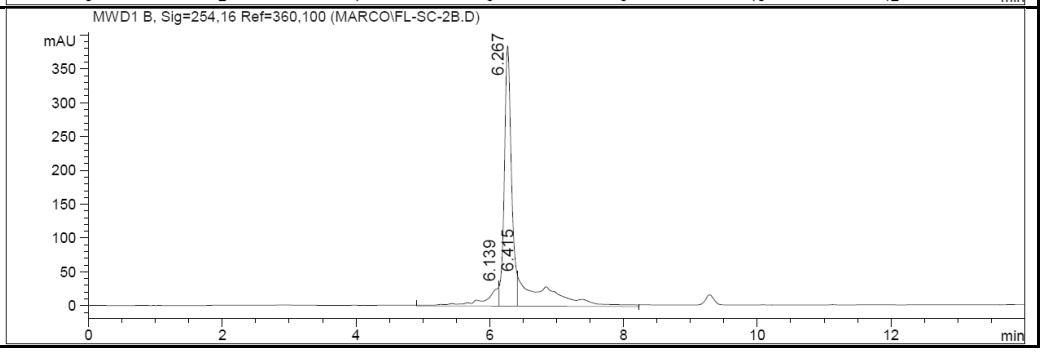
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $FeCl_2 \cdot 4\ H_2O$ (200 equiv., 4 µmol) in dry ACN.

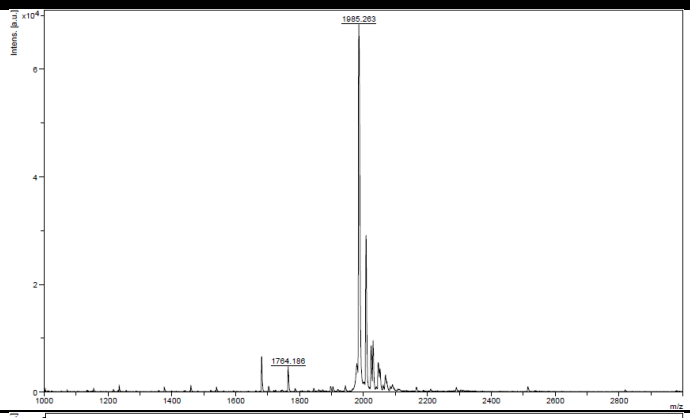
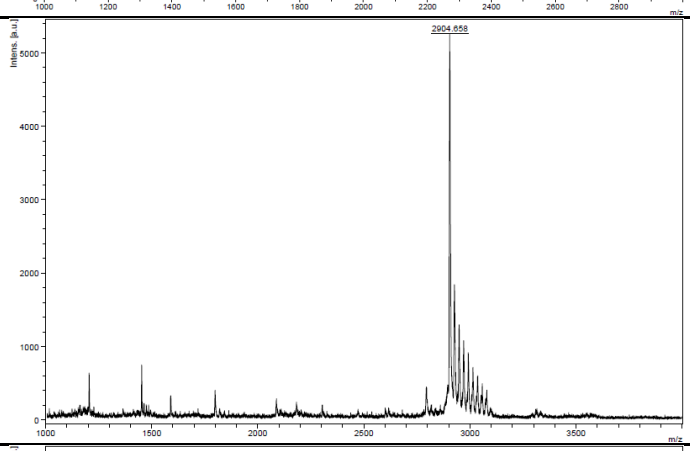
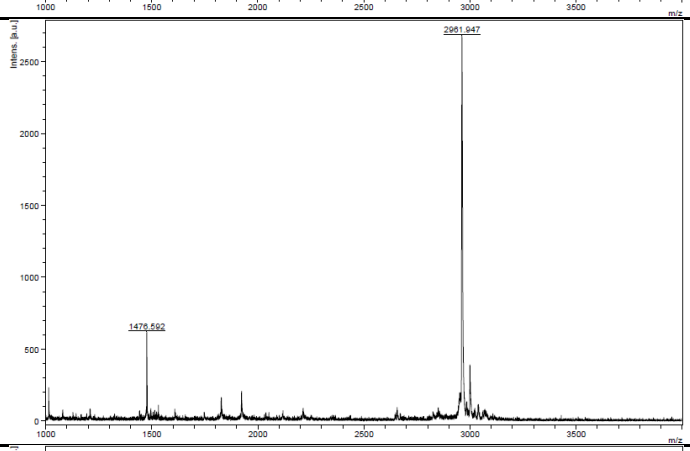
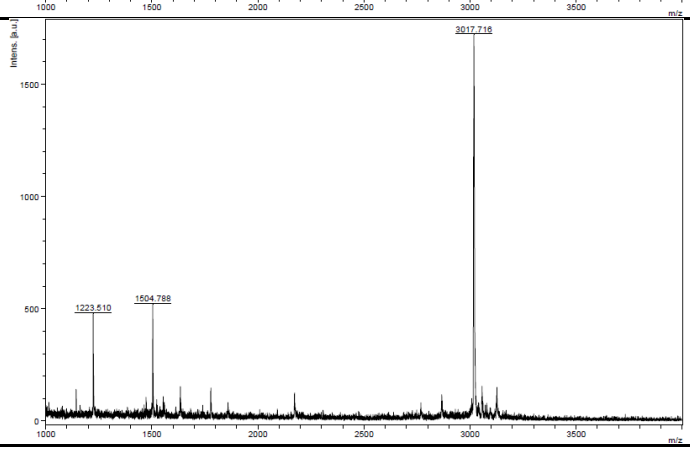
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.7

CPG-oligonucleotide + $InCl_3$

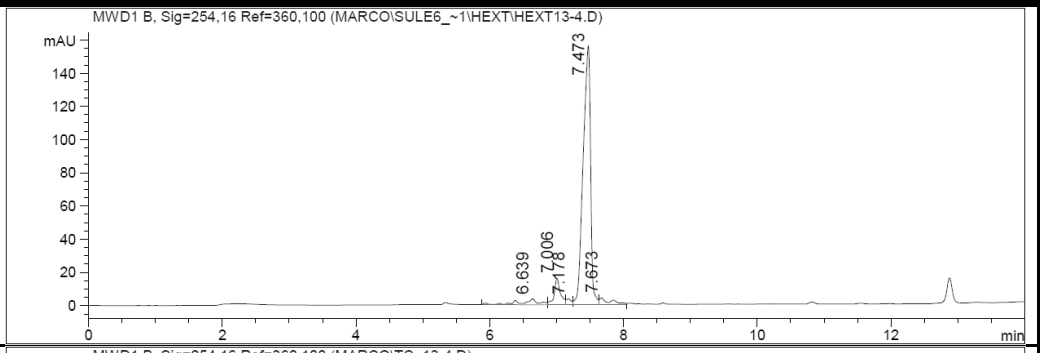
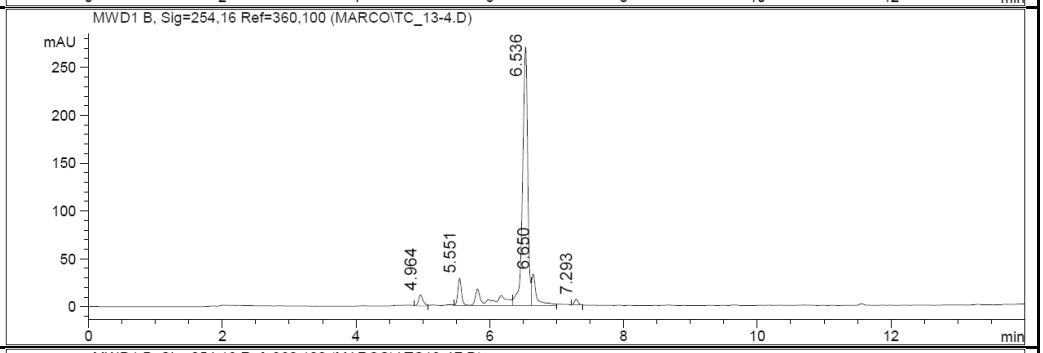
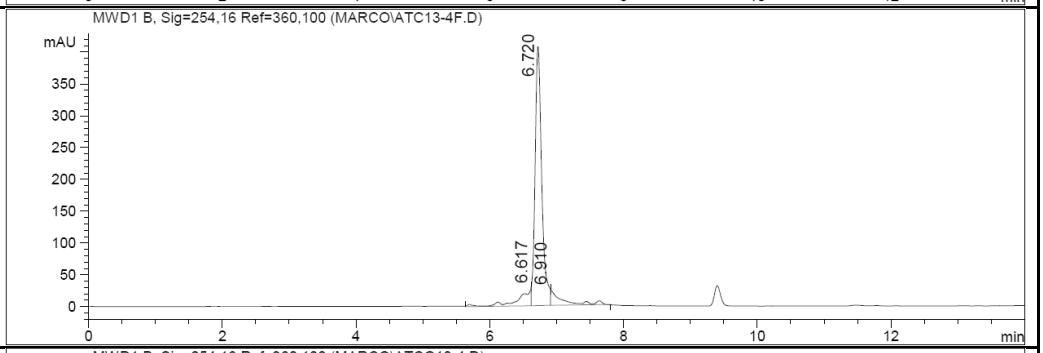
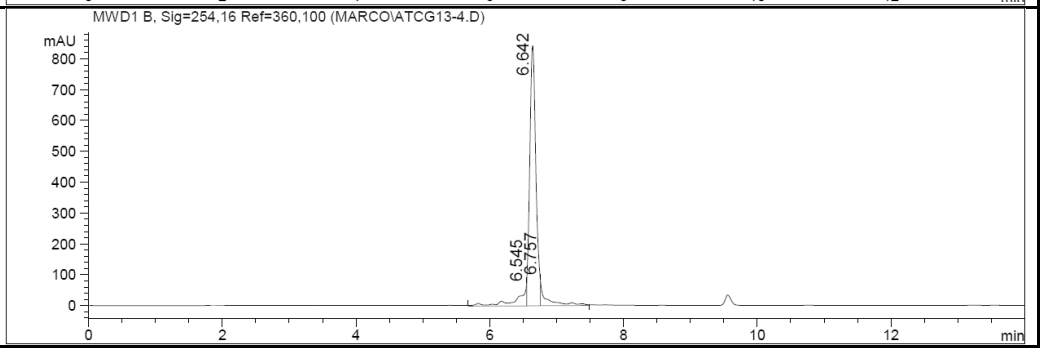
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $InCl_3$ (200 equiv., 4 µmol) in dry ACN.

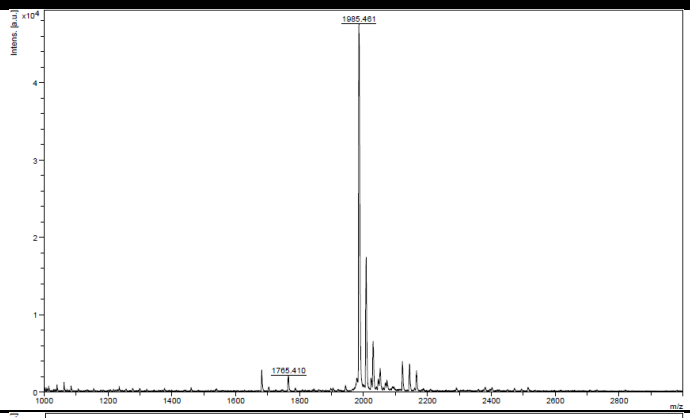
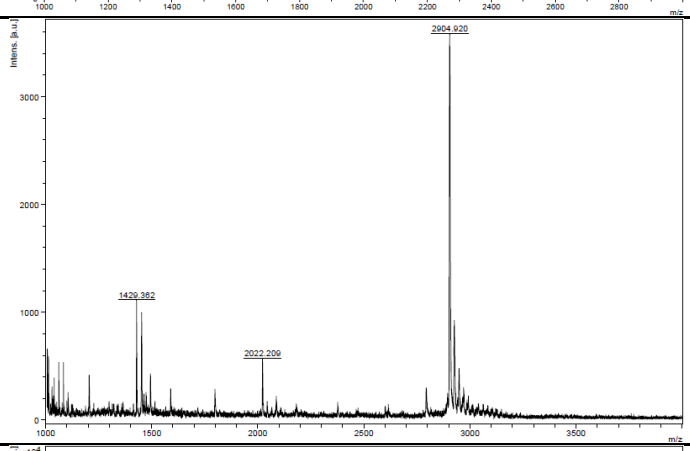
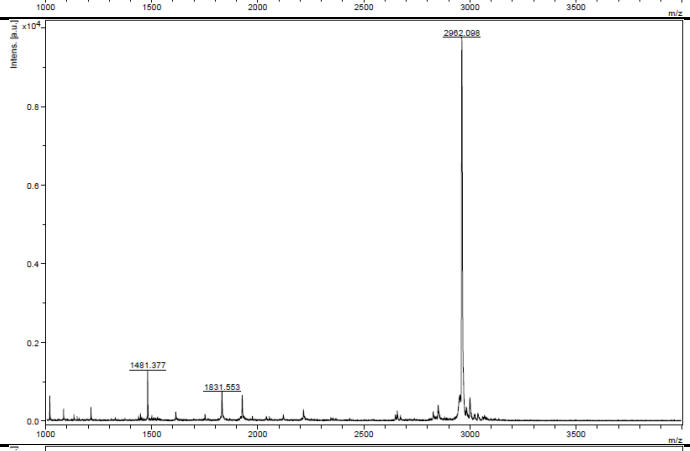
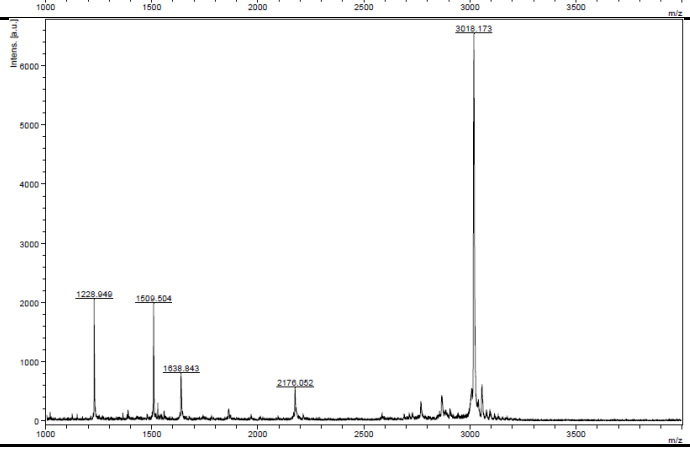
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.9
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.7

CPG-oligonucleotide + La(O*i*Pr)$_3$

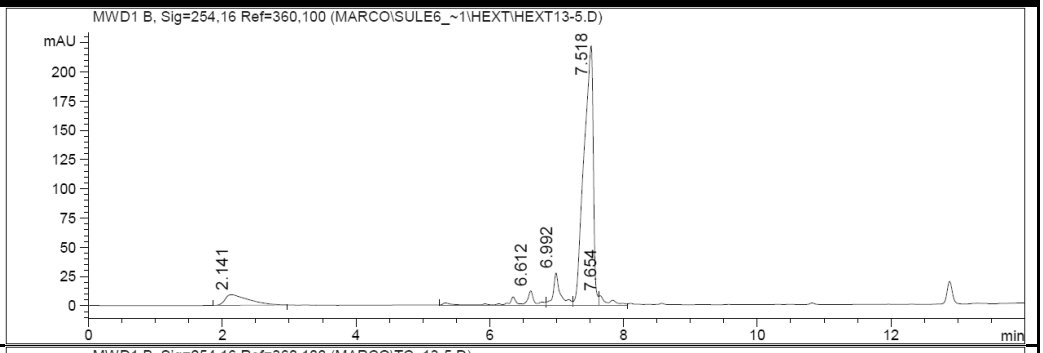
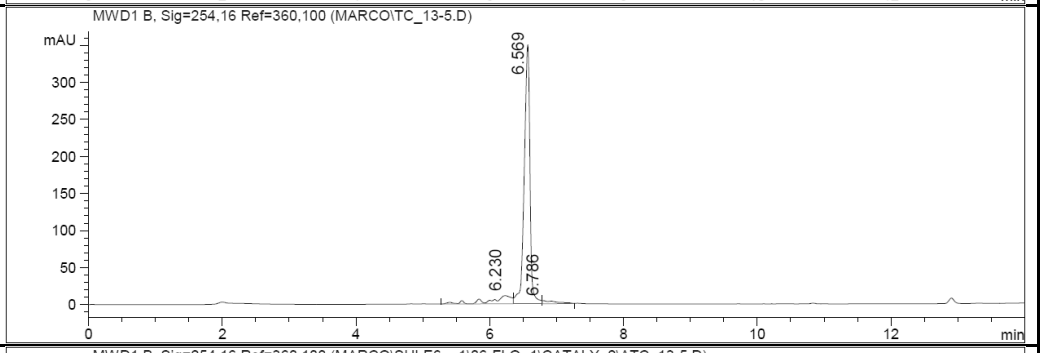
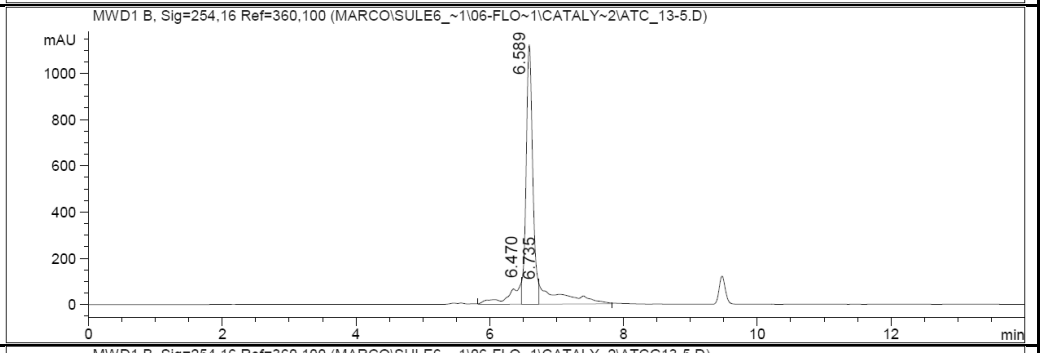
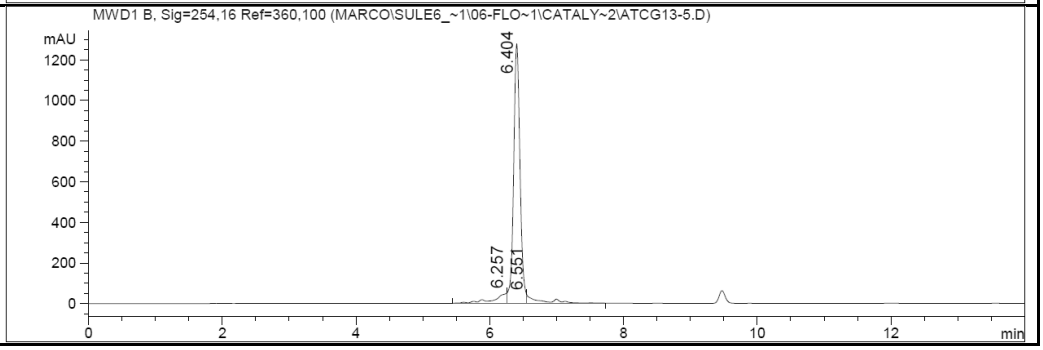
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with La(O*i*Pr)$_3$ (200 equiv., 4 µmol) in dry THF.

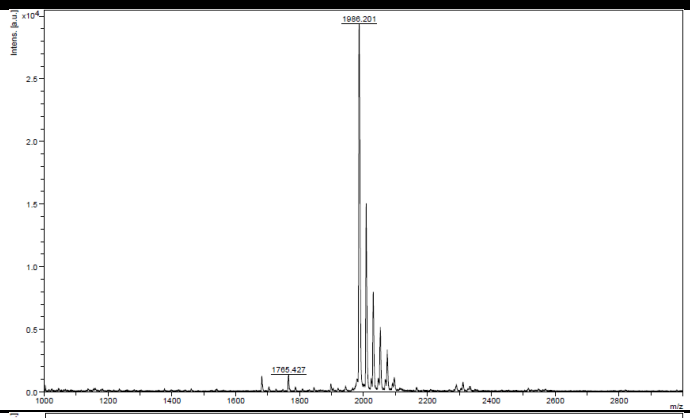
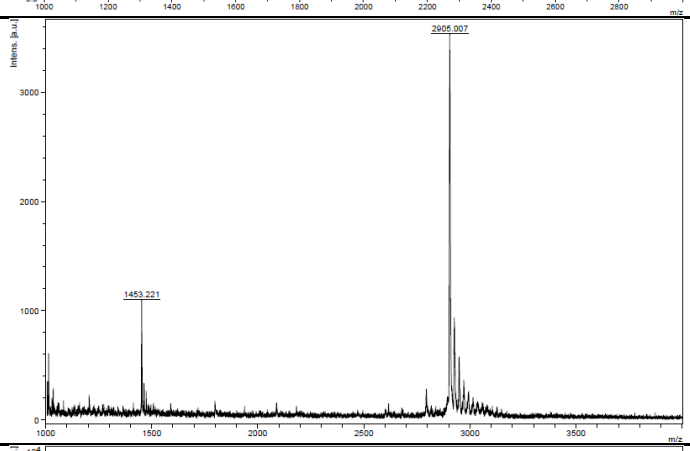
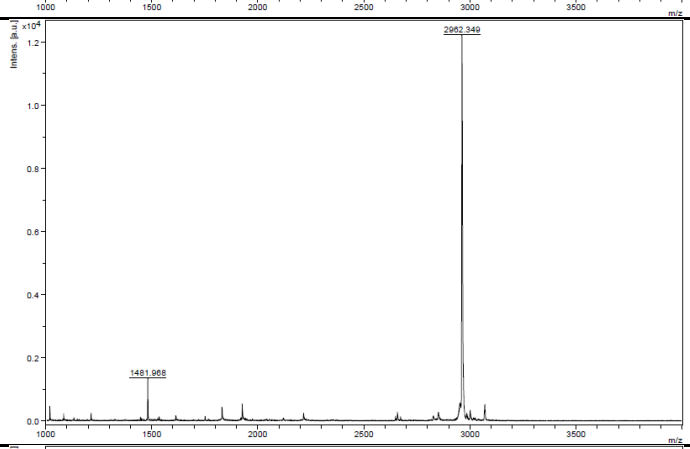
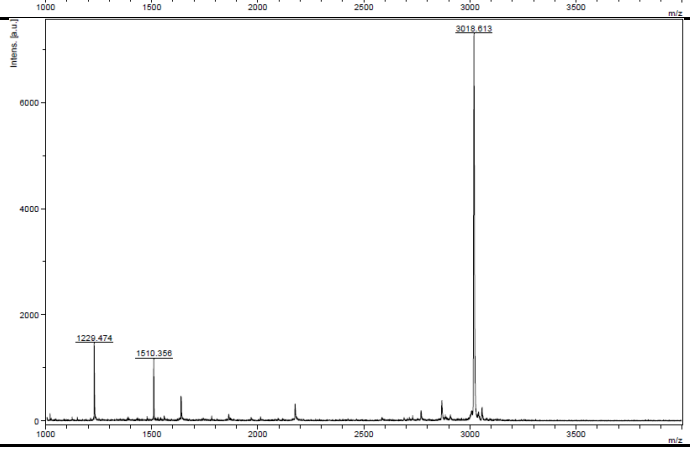
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.5
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.1
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.2

CPG-oligonucleotide + LiBr

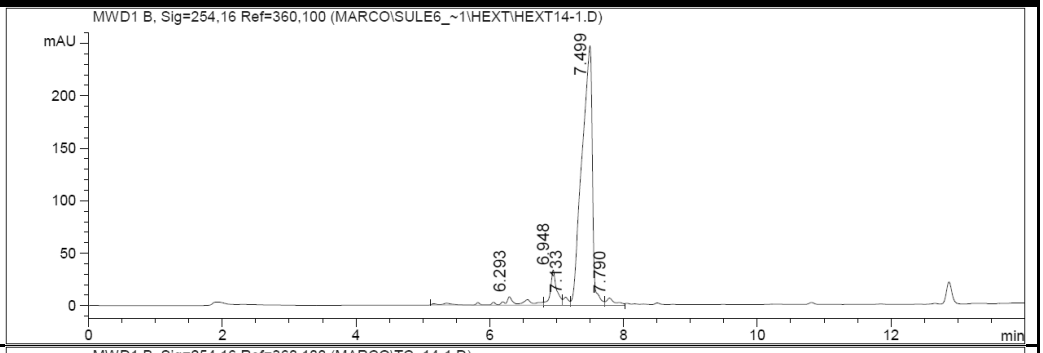
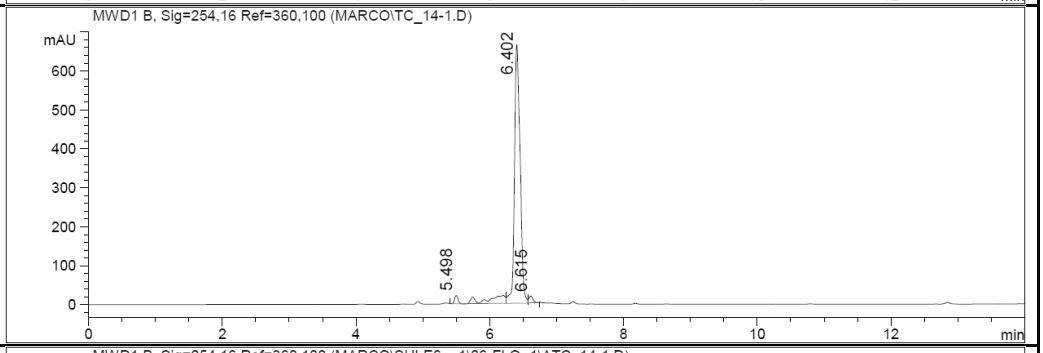
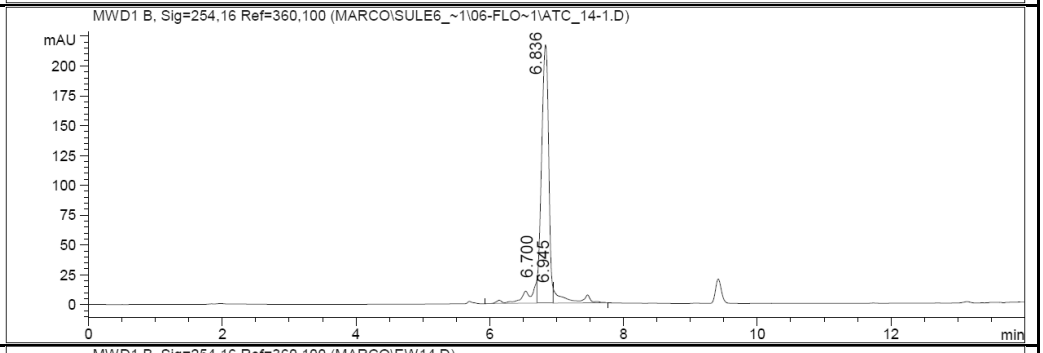
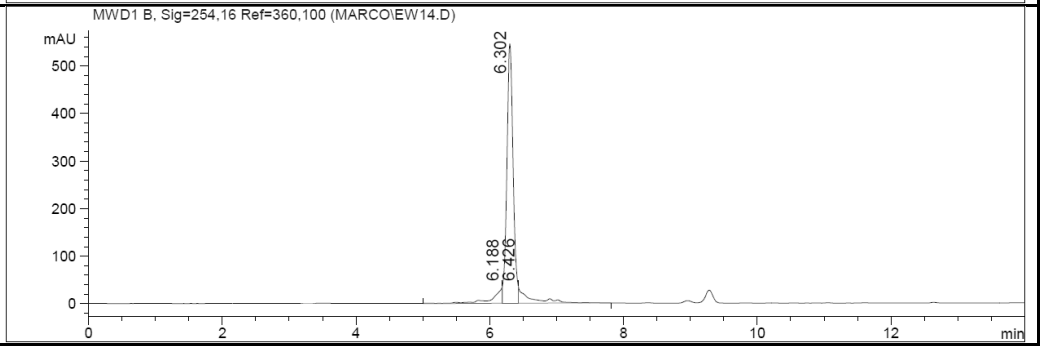
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with LiBr (200 equiv., 4 µmol) in dry ACN.

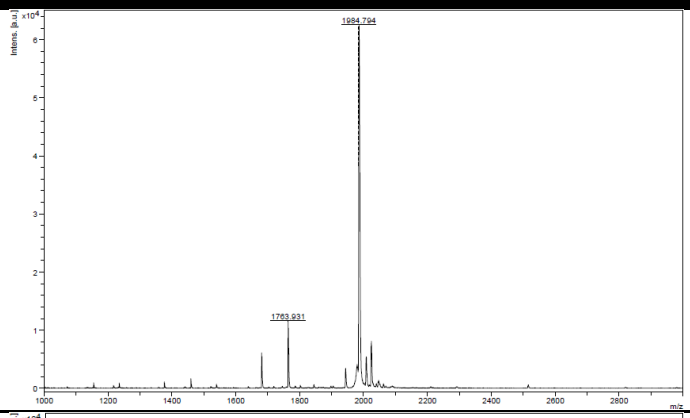
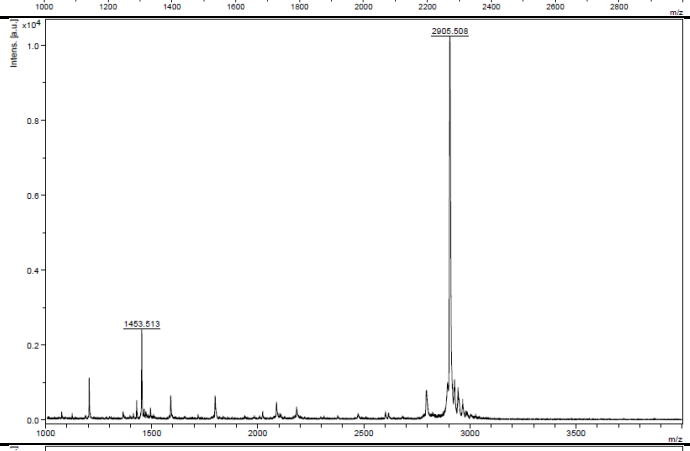
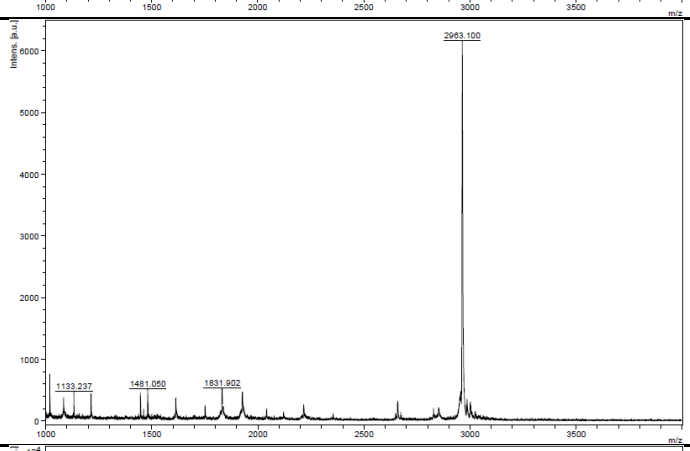
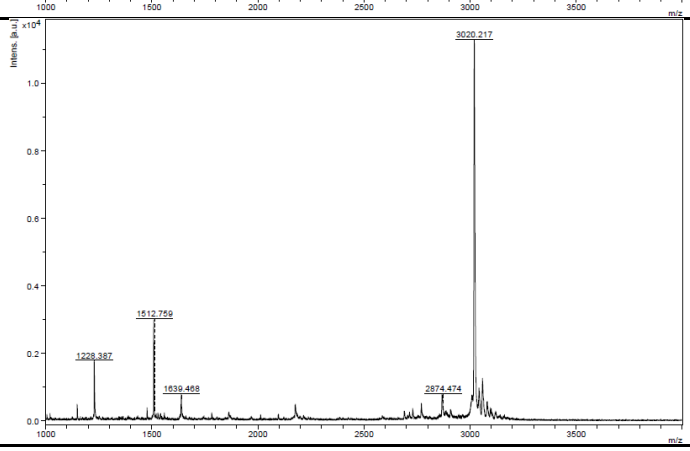
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.0
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

CPG-oligonucleotide + $Mg(ClO_4)_2$

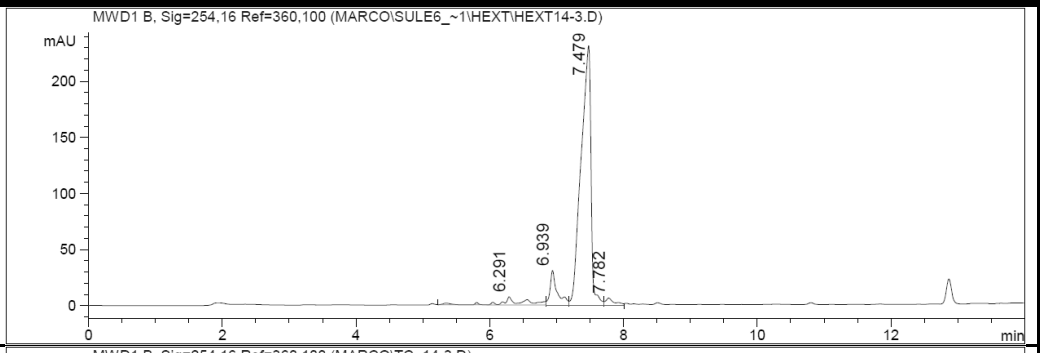
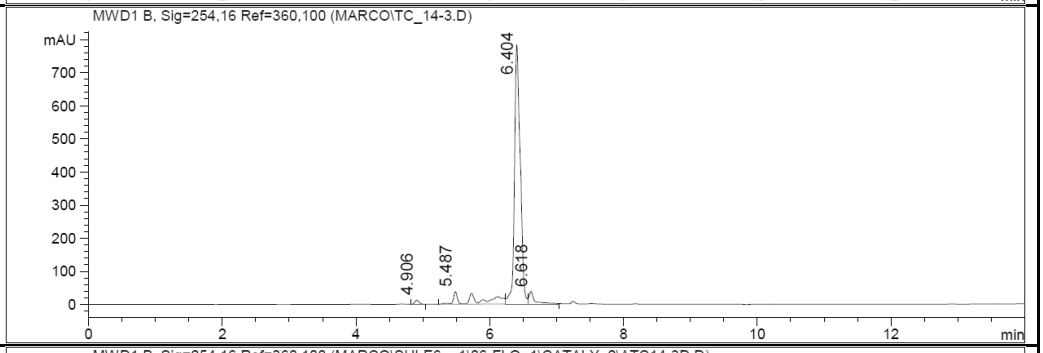
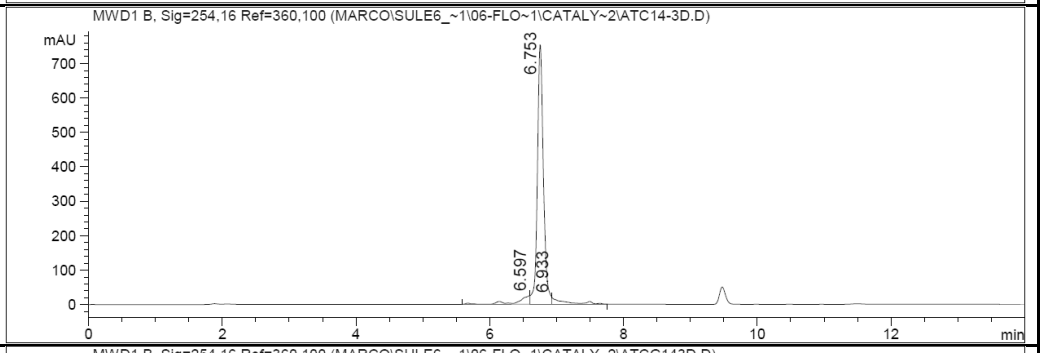
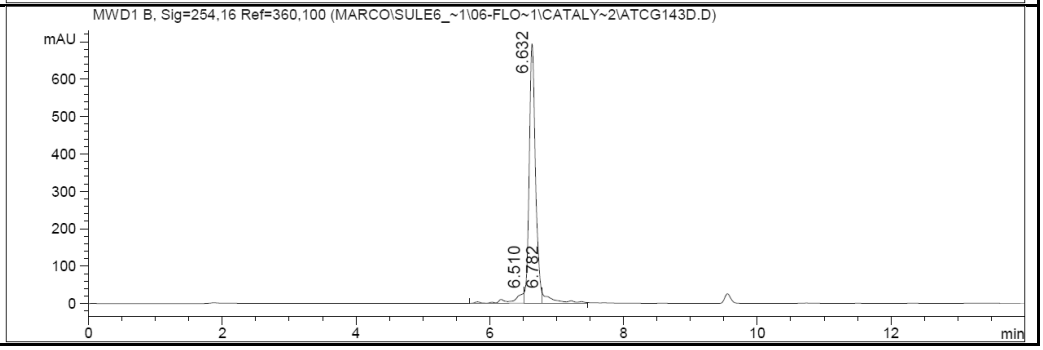
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Mg(ClO_4)_2$ (200 equiv., 4 µmol) in dry MeOH.

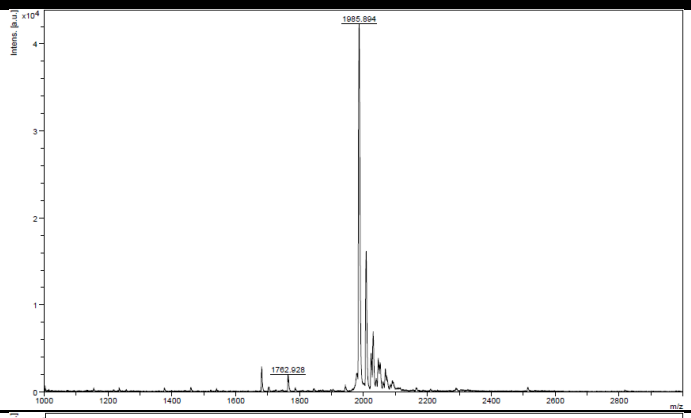
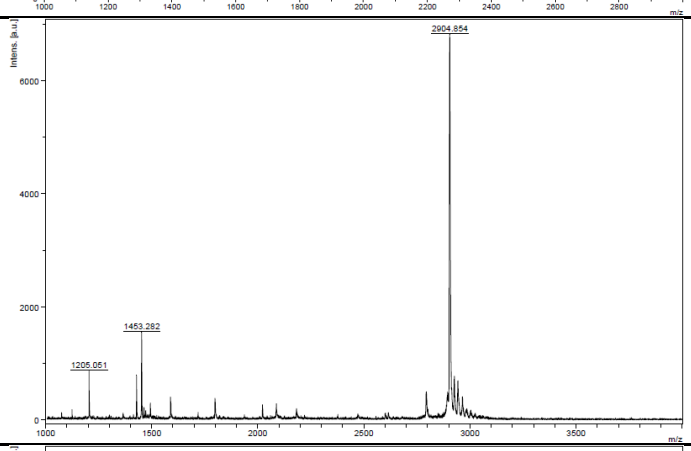
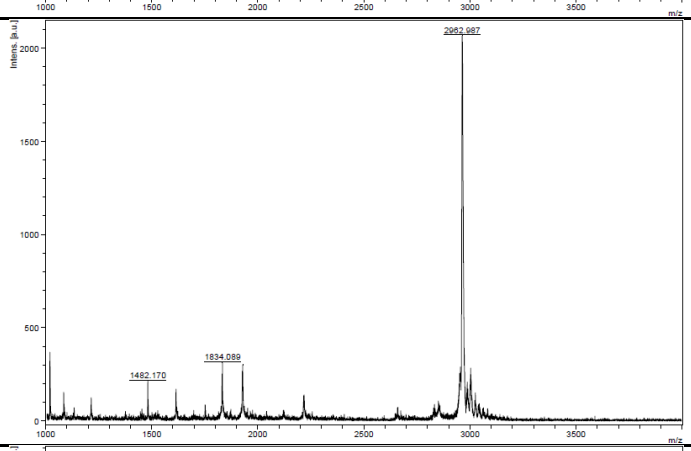
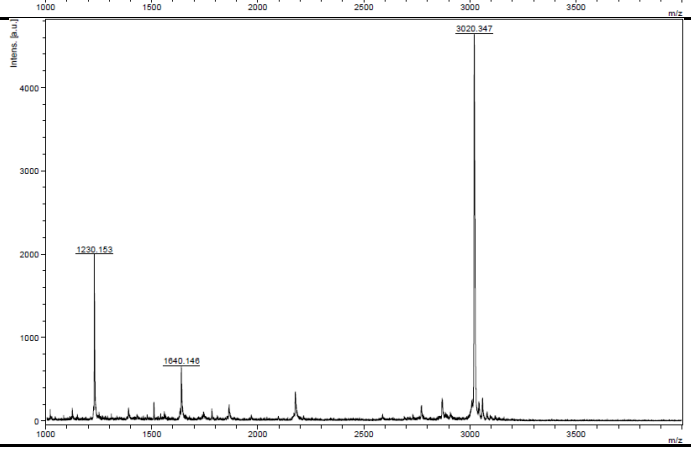
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1984.8
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.5
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.1
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3020.2

CPG-oligonucleotide + Ni(acac)$_2$

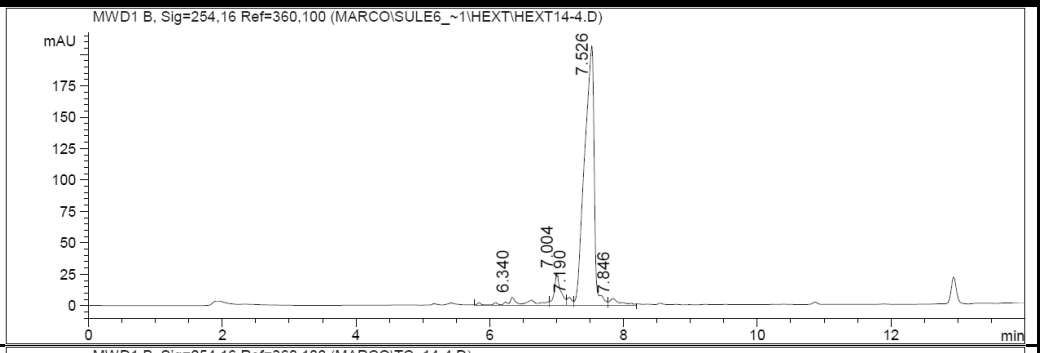
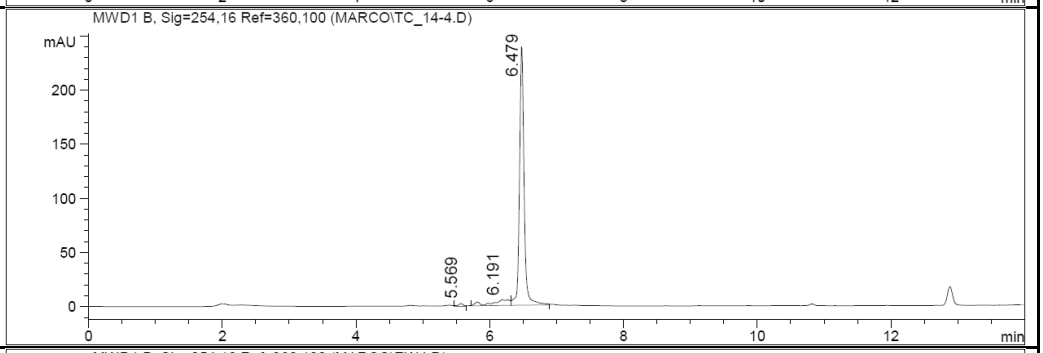
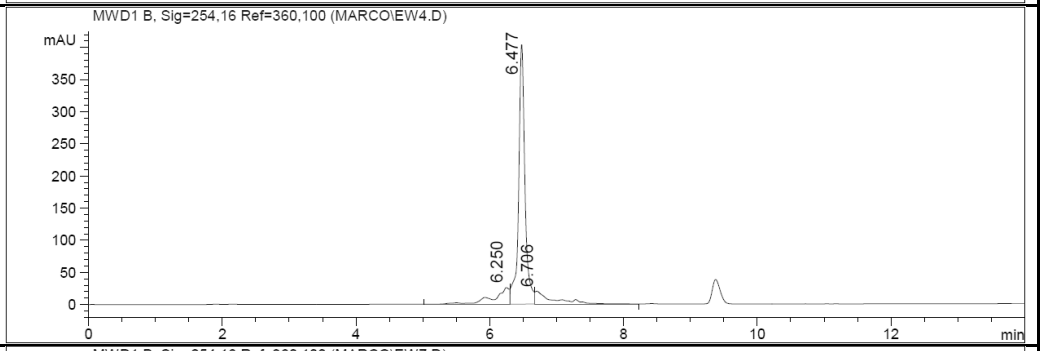
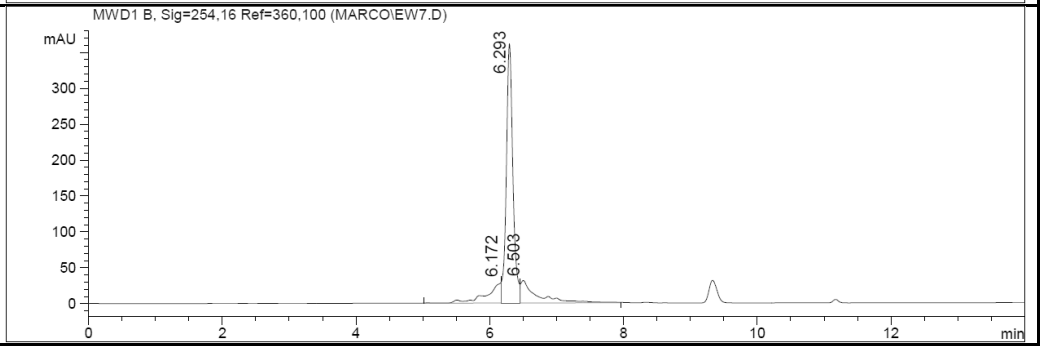
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with Ni(acac)$_2$ (200 equiv., 4 µmol) in dry ACN.

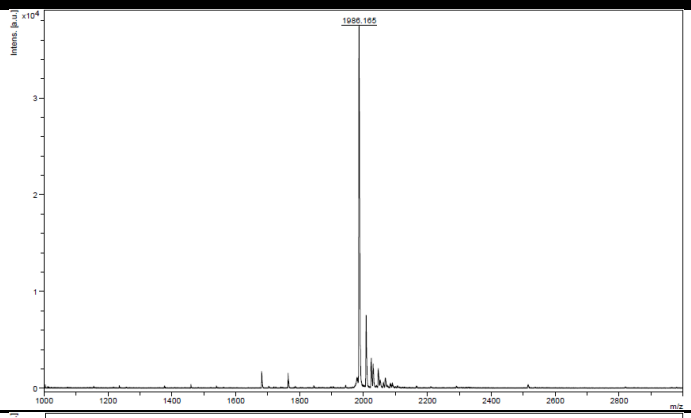
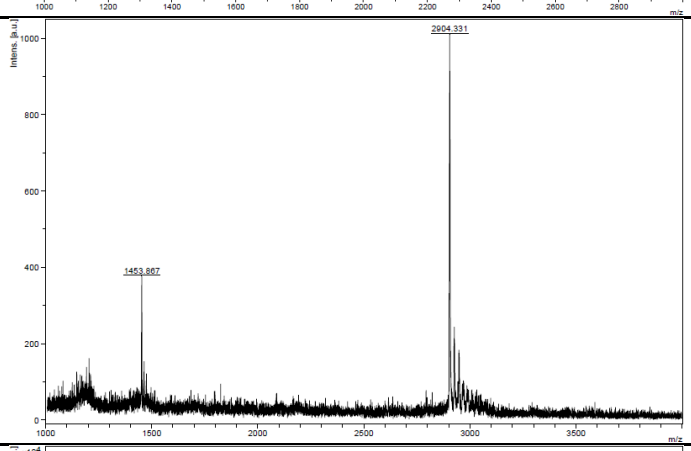
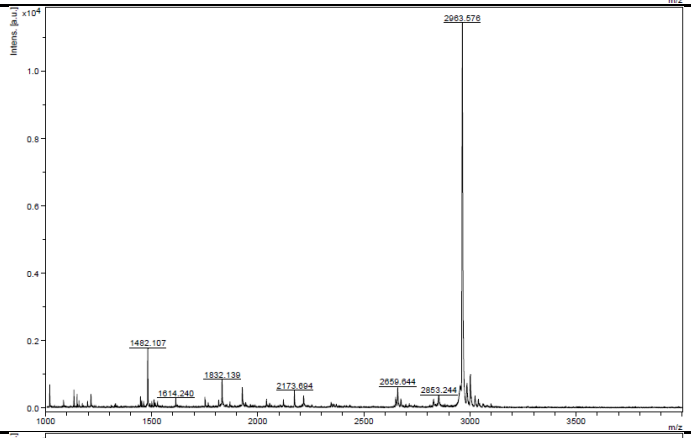
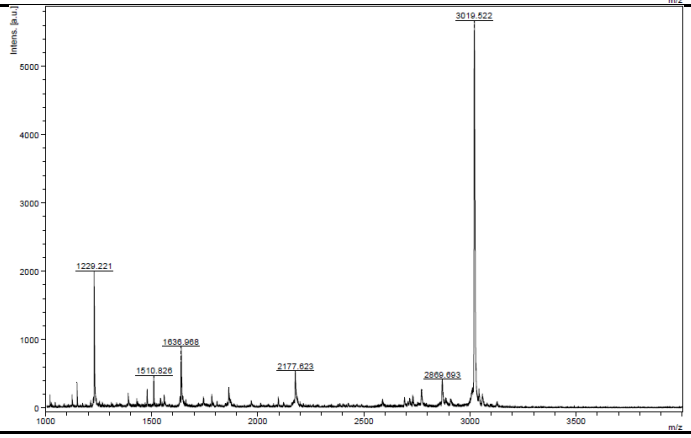
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-(CH$_2$)$_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.9
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3020.3

CPG-oligonucleotide + $Ni(PPh_3)_2Cl_2$

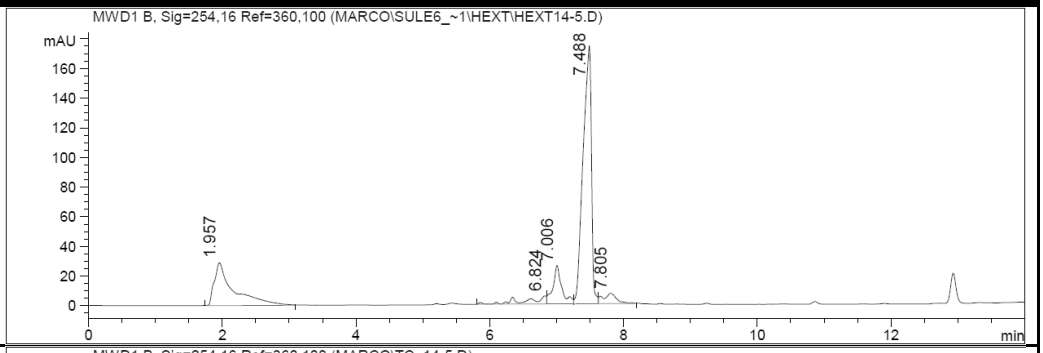
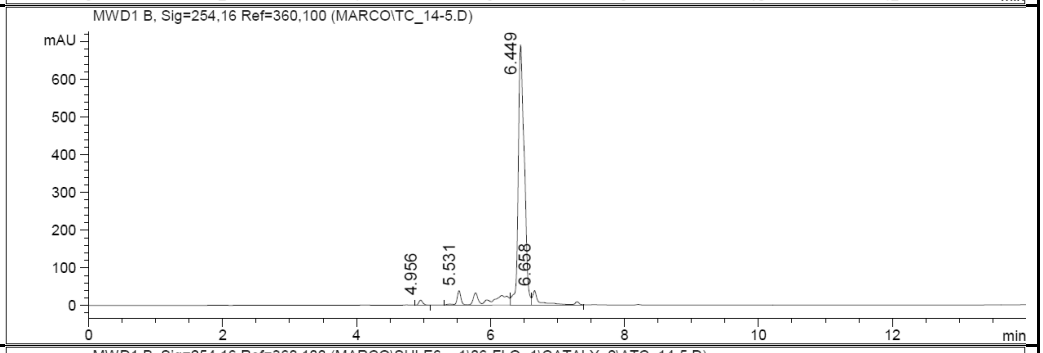
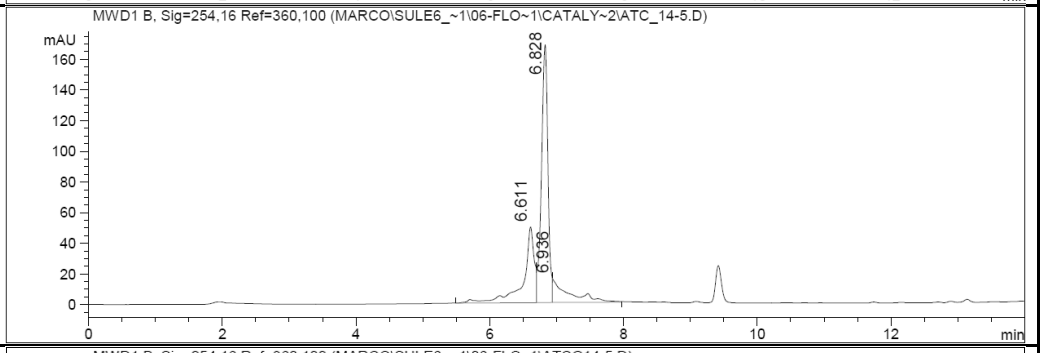
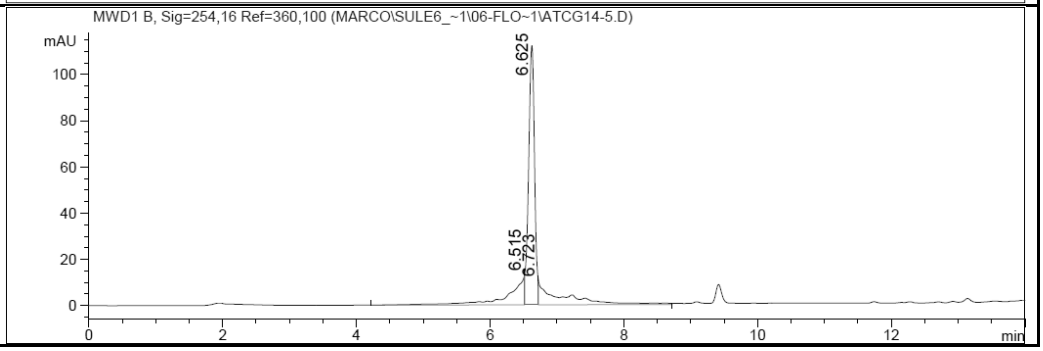
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Ni(PPh_3)_2Cl_2$ (200 equiv., 4 µmol) in dry MeOH.

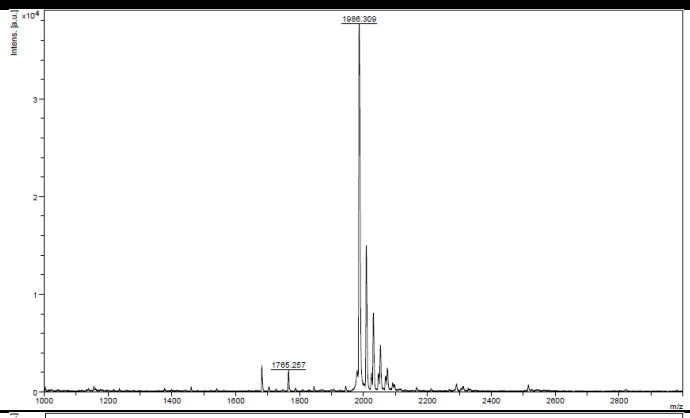
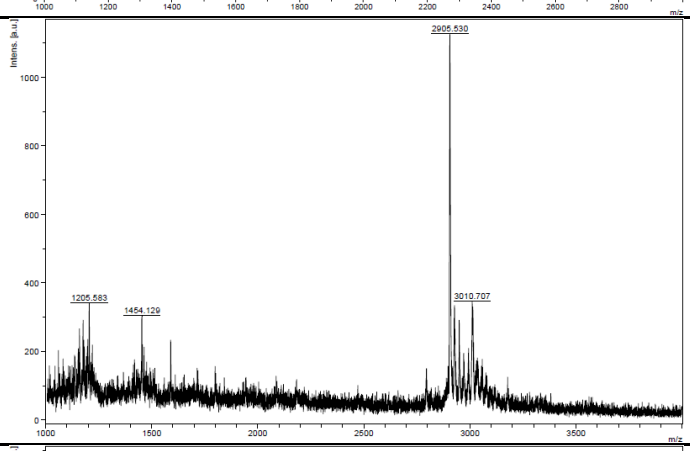
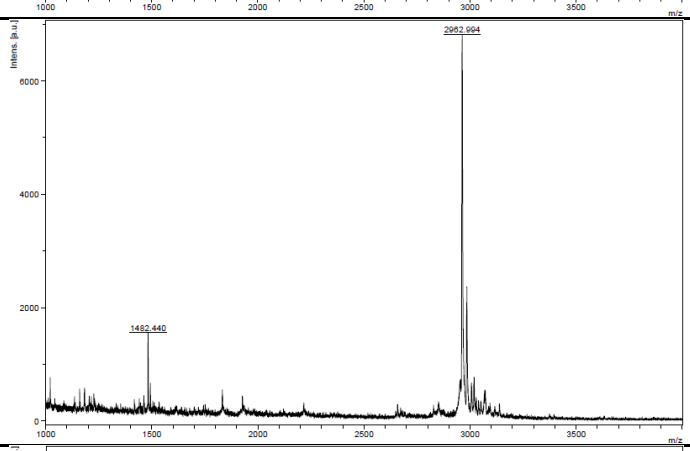
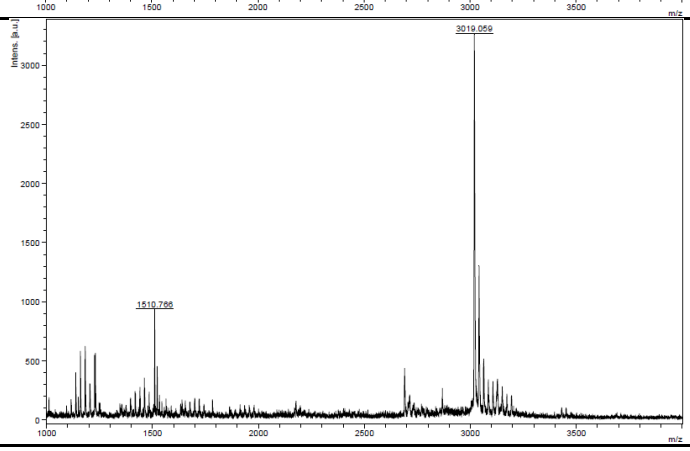
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **$AcNH-(CH_2)_6-$** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.3
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.6
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.5

CPG-oligonucleotide + $Pd(dba)_3$

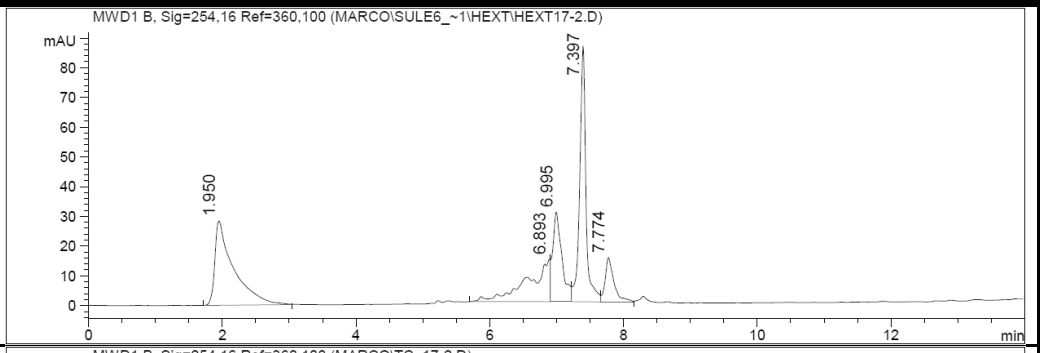
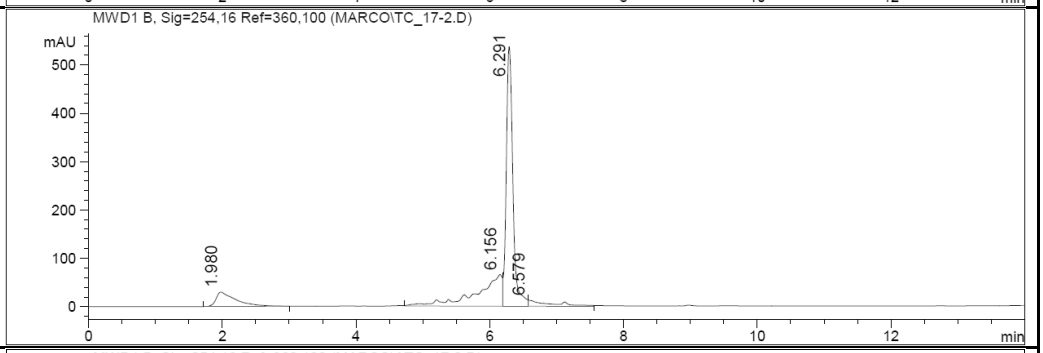
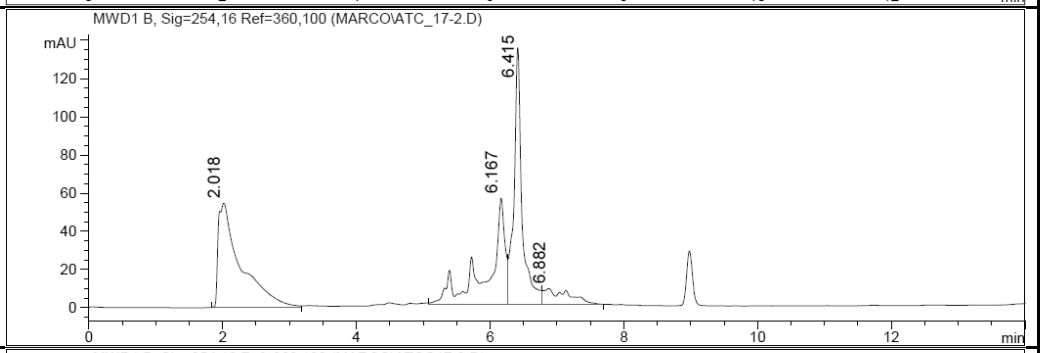
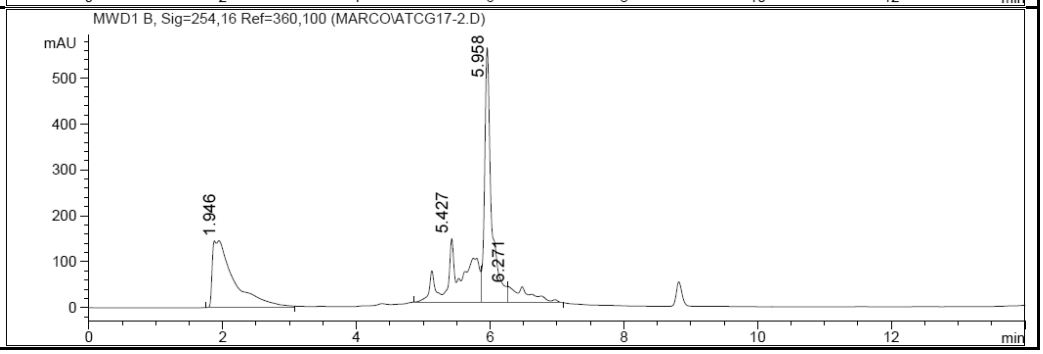
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Pd(dba)_3$ (200 equiv., 4 µmol) in dry MeOH.

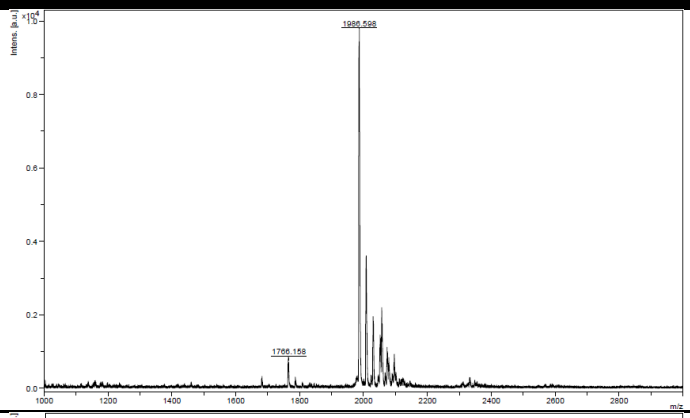
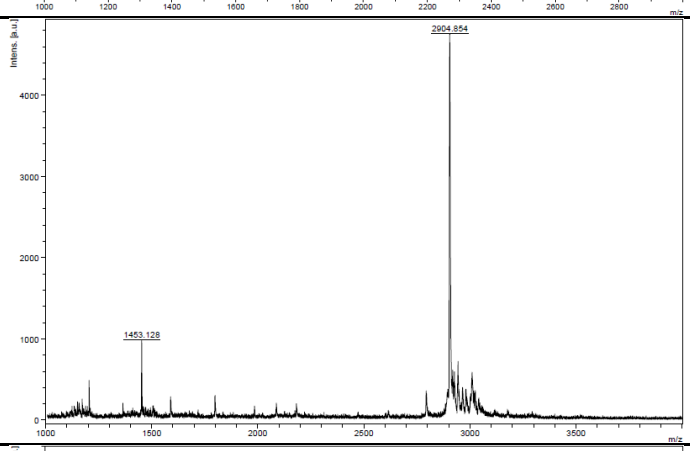
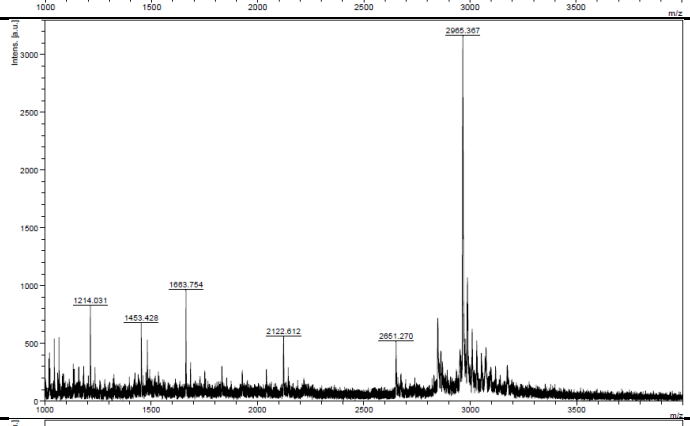
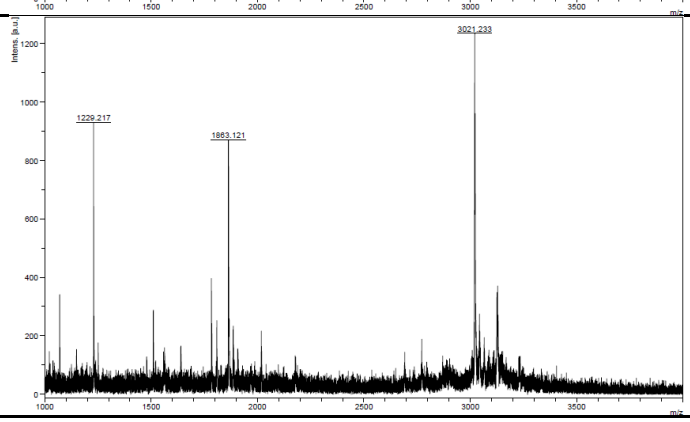
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.5
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.1

CPG-oligonucleotide + $Pd(OAc)_2$

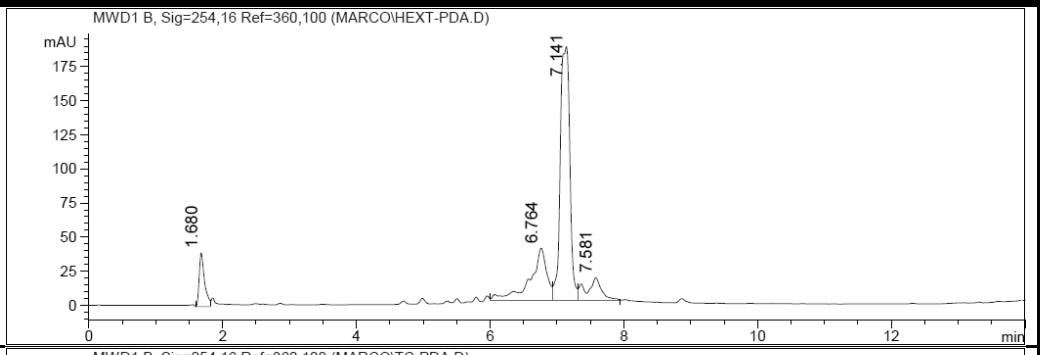
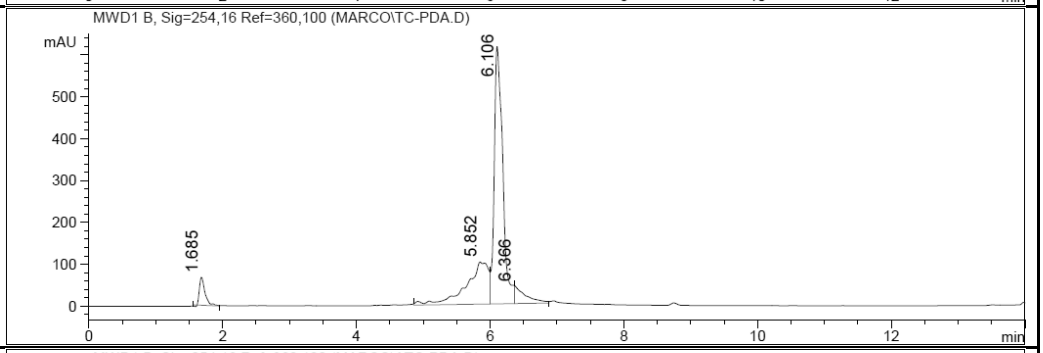
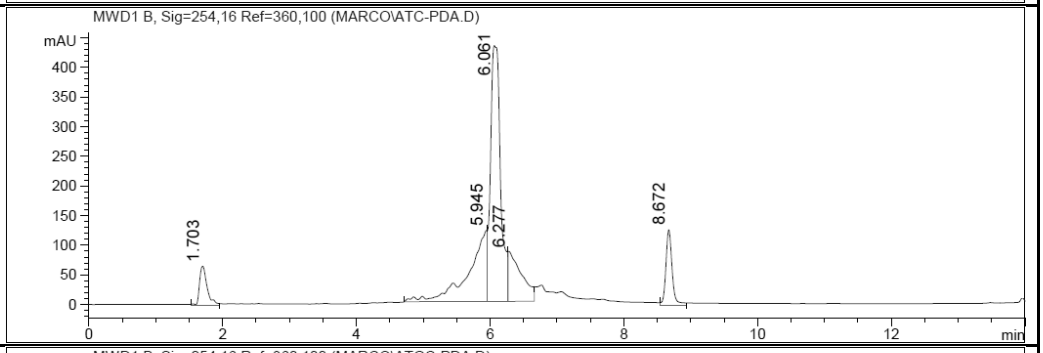
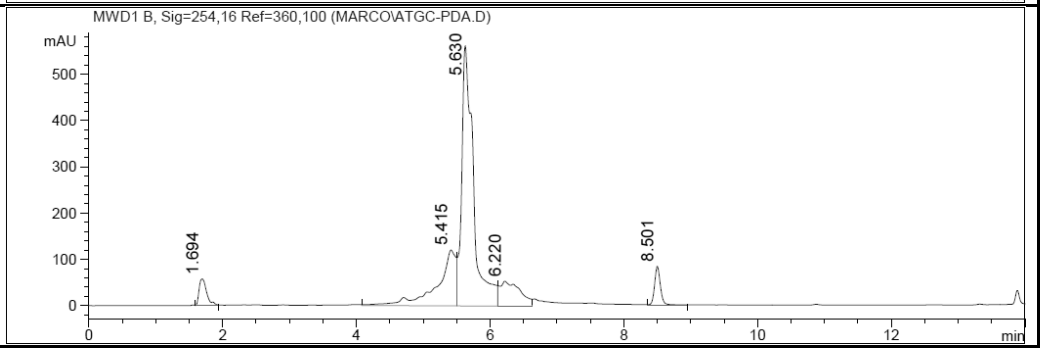
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Pd(OAc)_2$ (200 equiv., 4 µmol) in dry ACN.

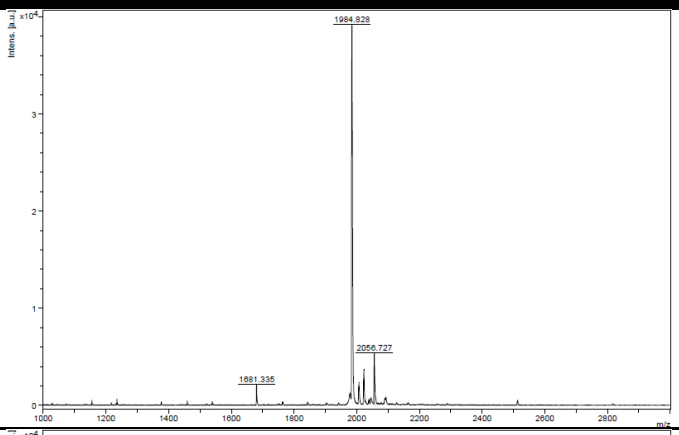
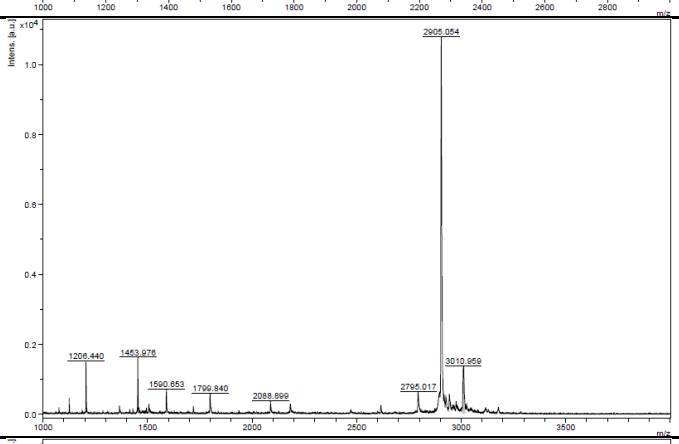
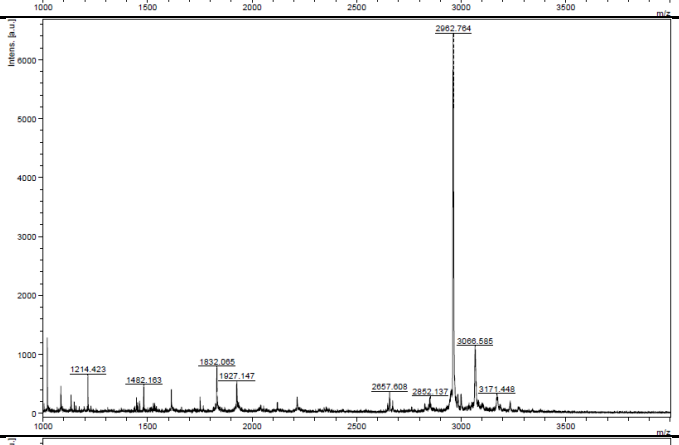
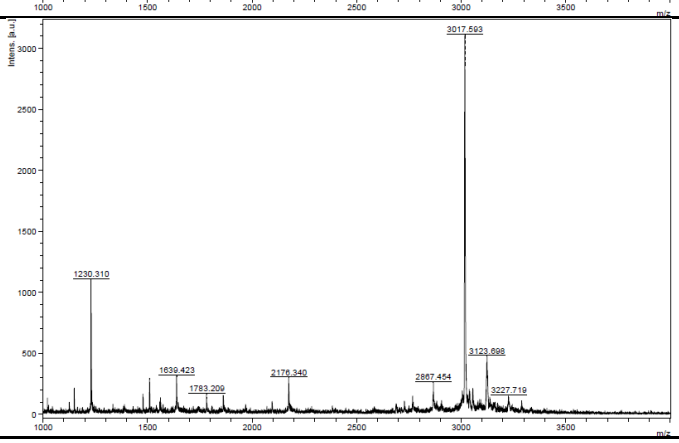
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2965.4
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3021.2

CPG-oligonucleotide + $Pd(OAc)_2$

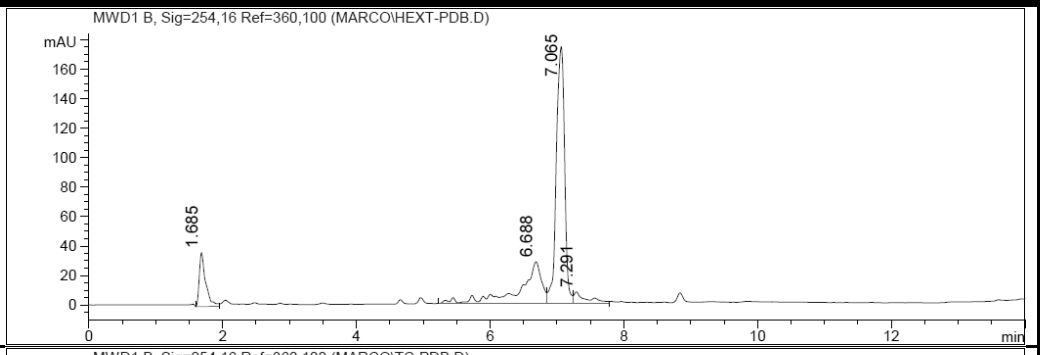
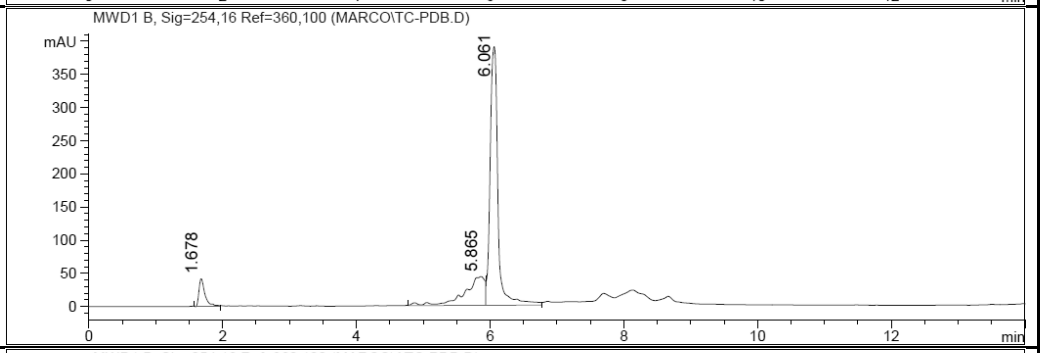
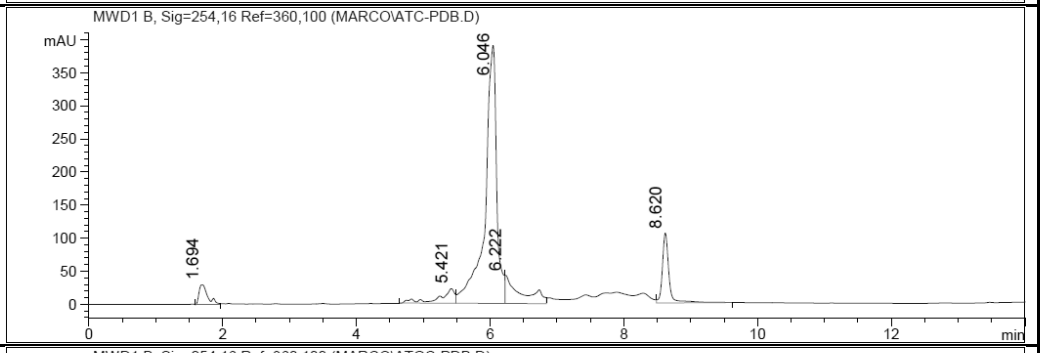
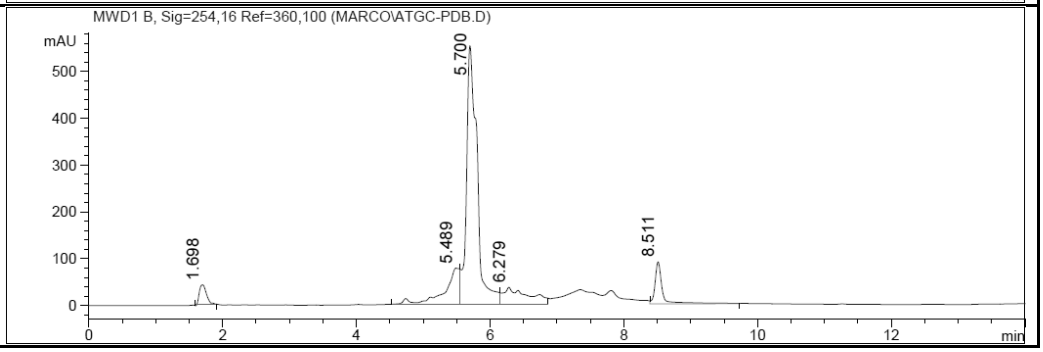
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Pd(OAc)_2$ (5 equiv., 0.1 µmol) in dry ACN.

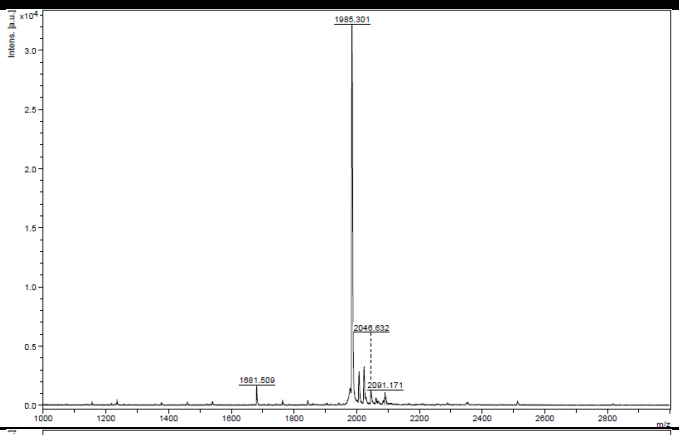
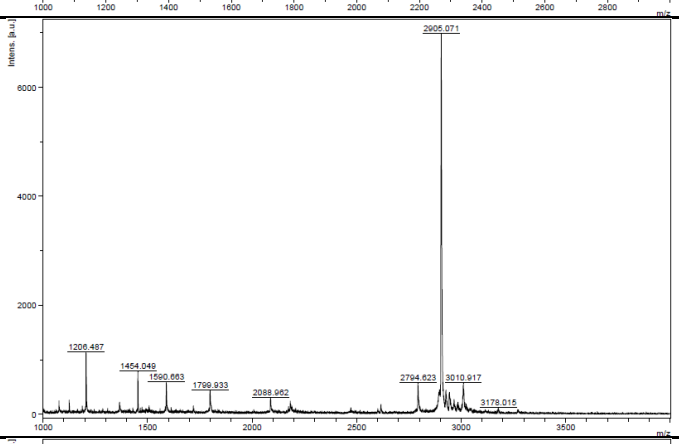
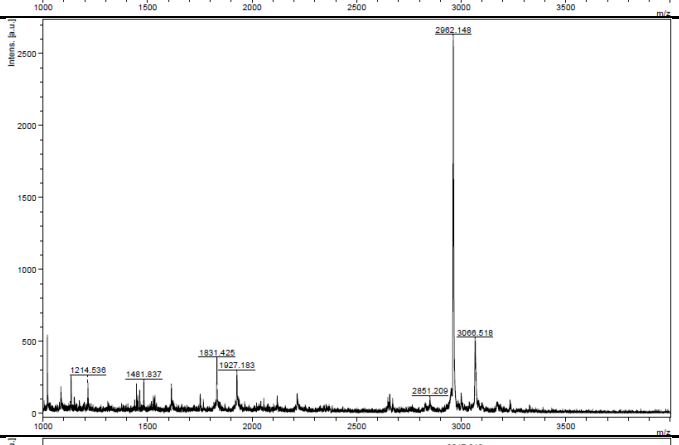
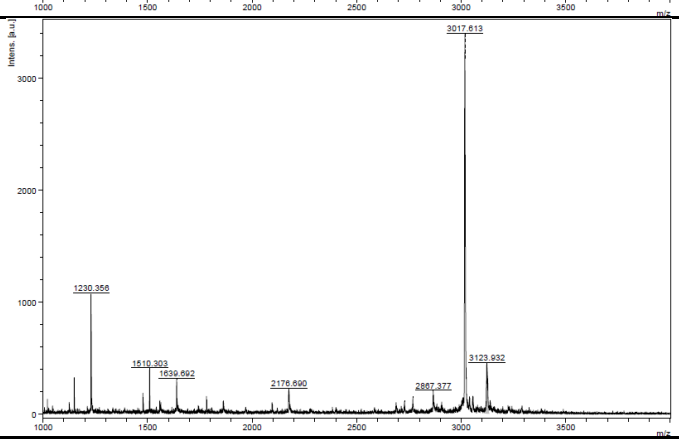
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1984.8
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.1
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.6

CPG-oligonucleotide + $Pd(PPh_3)_4$

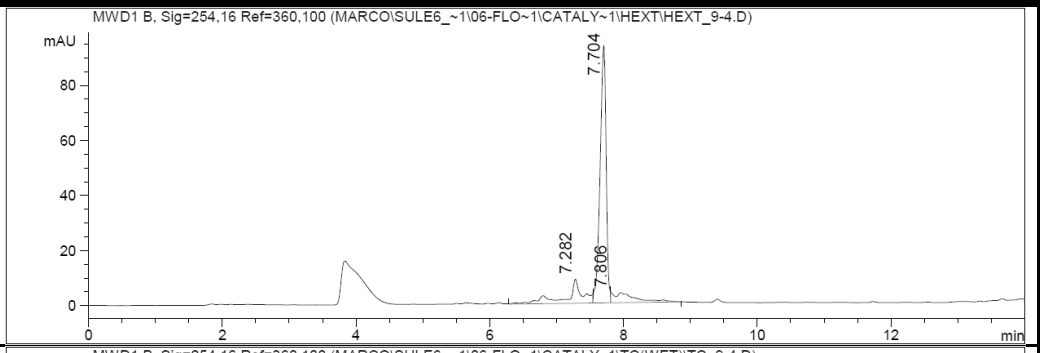
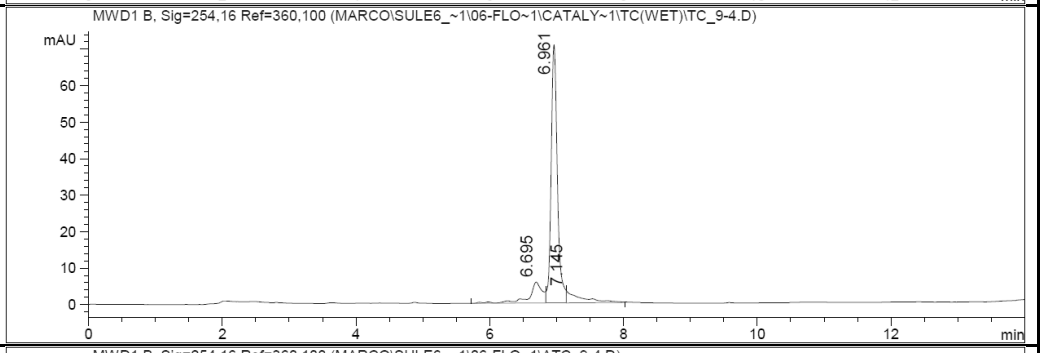
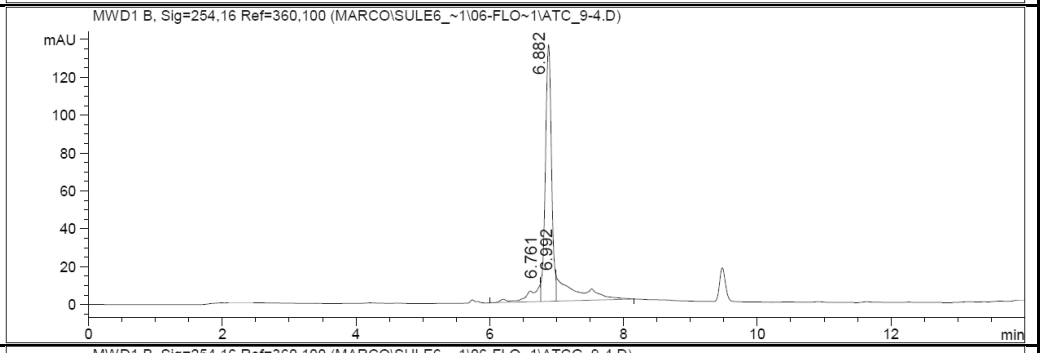
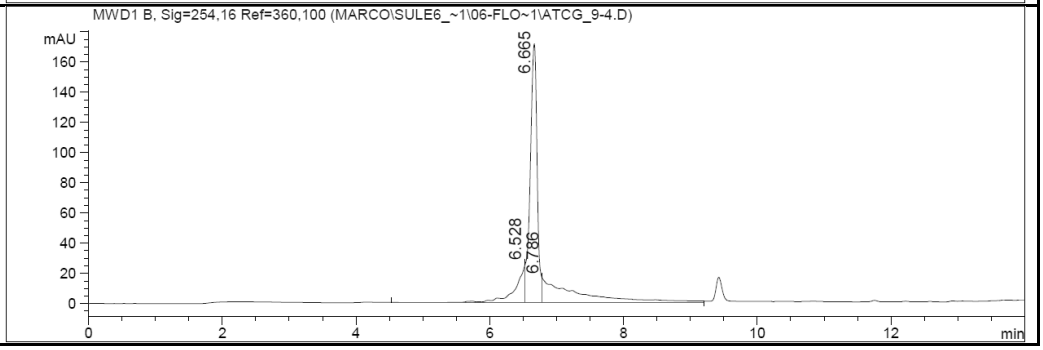
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Pd(PPh_3)_4$ (5 equiv., 0.1 µmol) in dry MeOH.

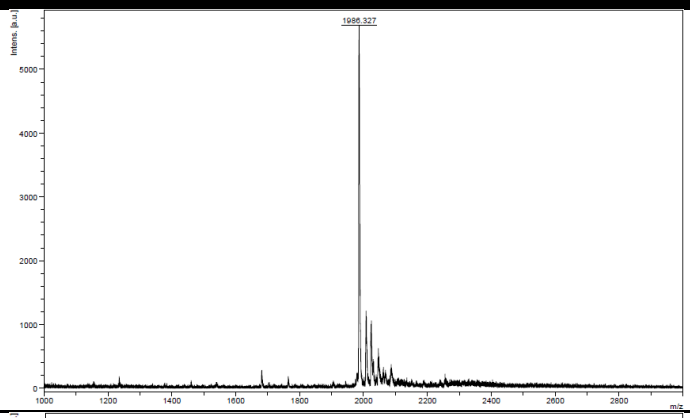
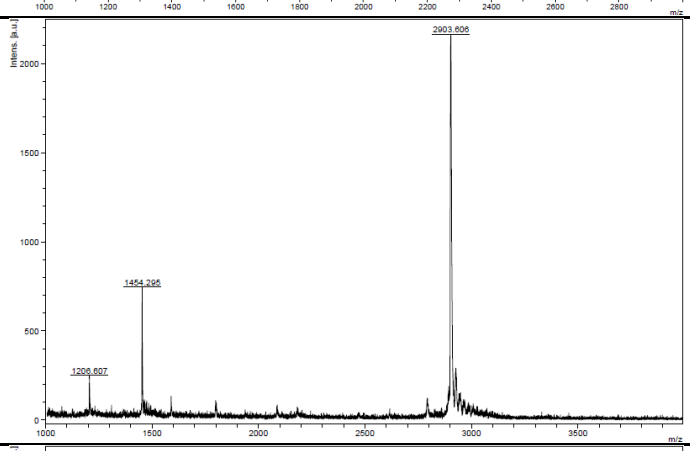
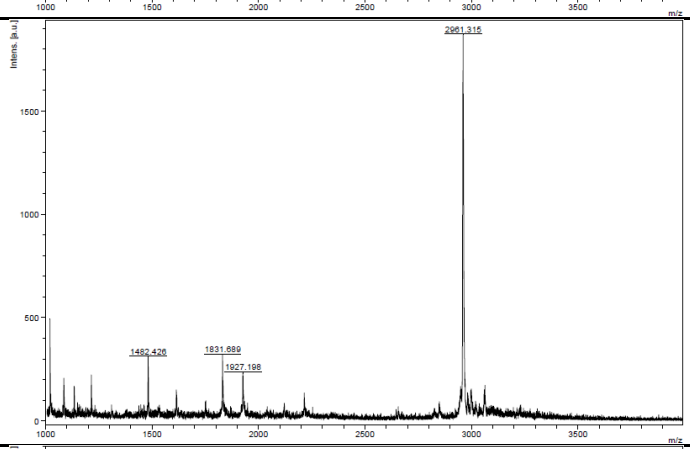
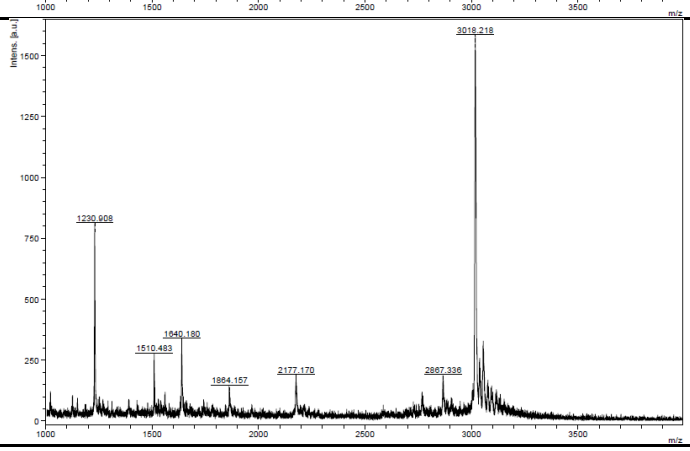
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.1
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.1
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.6

CPG-oligonucleotide + $[Rh(cod)Cl]_2$

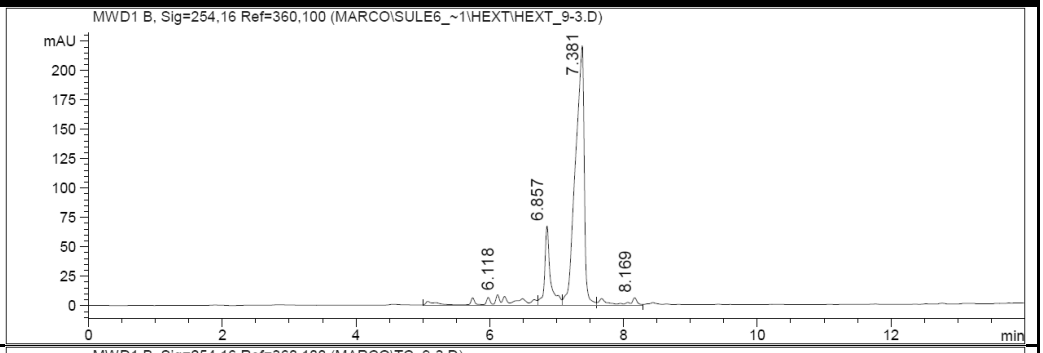
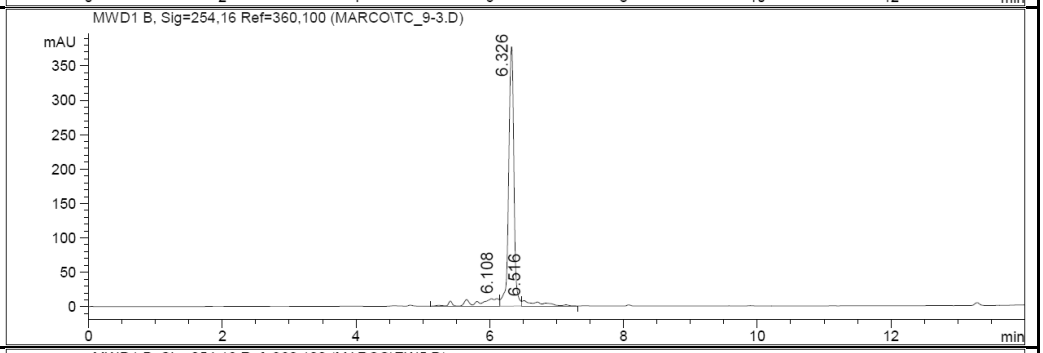
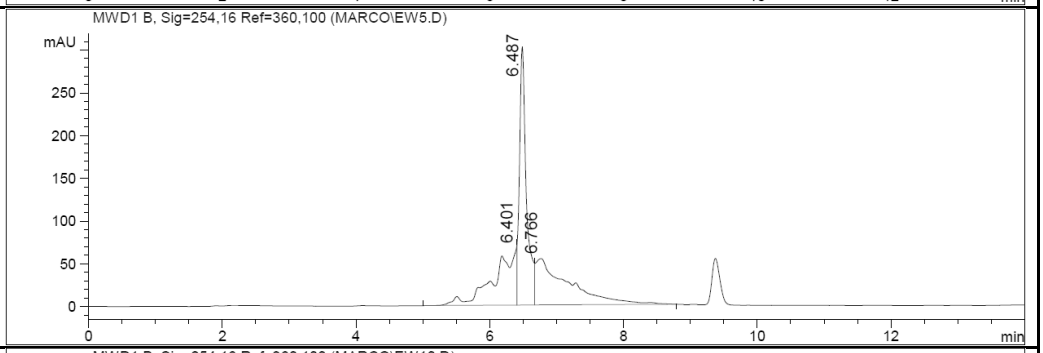
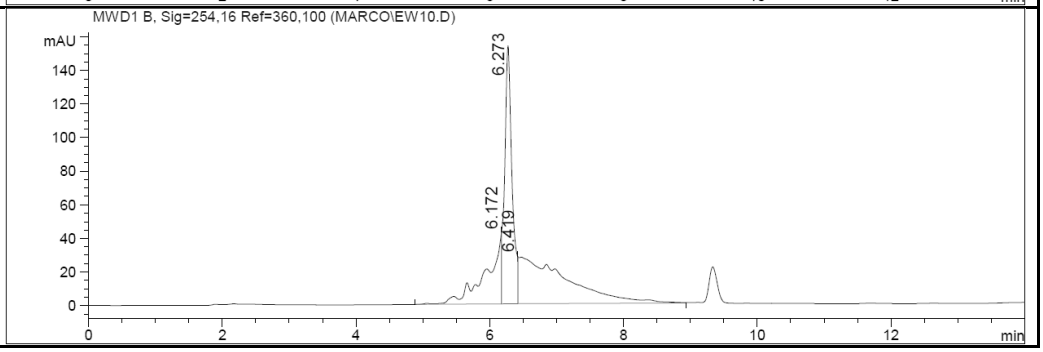
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $[Rh(cod)Cl]_2$ (200 equiv., 4 µmol) in dry MeOH.

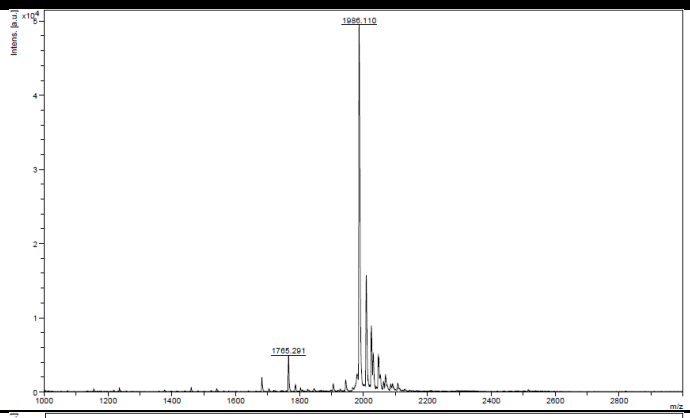
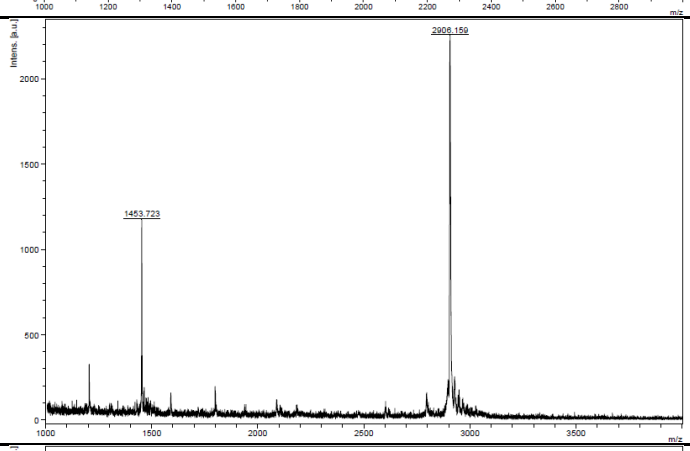
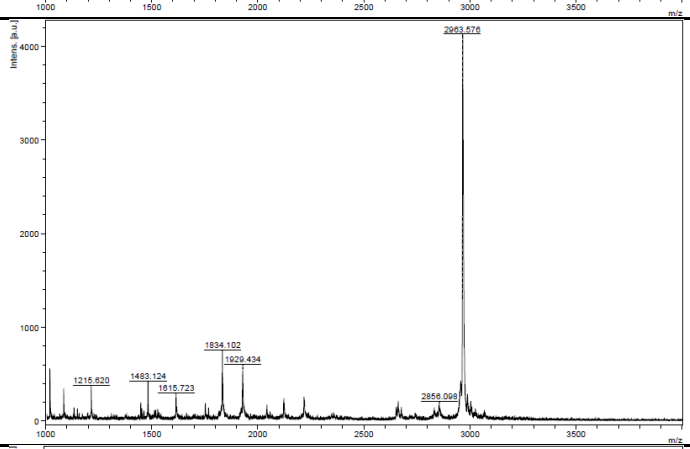
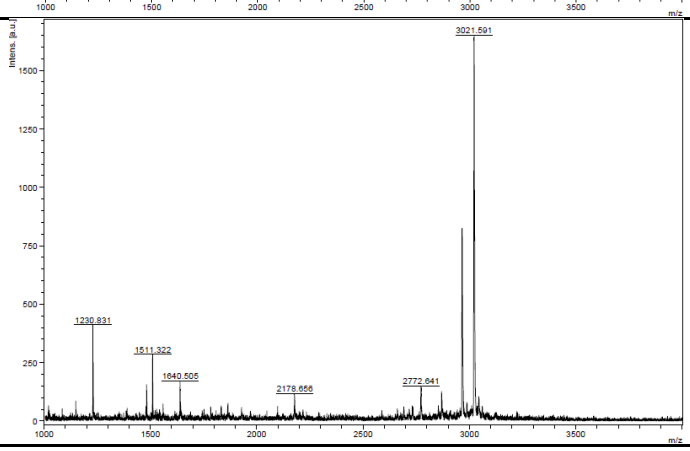
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2903.6
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.2

CPG-oligonucleotide + $RuCl_3$

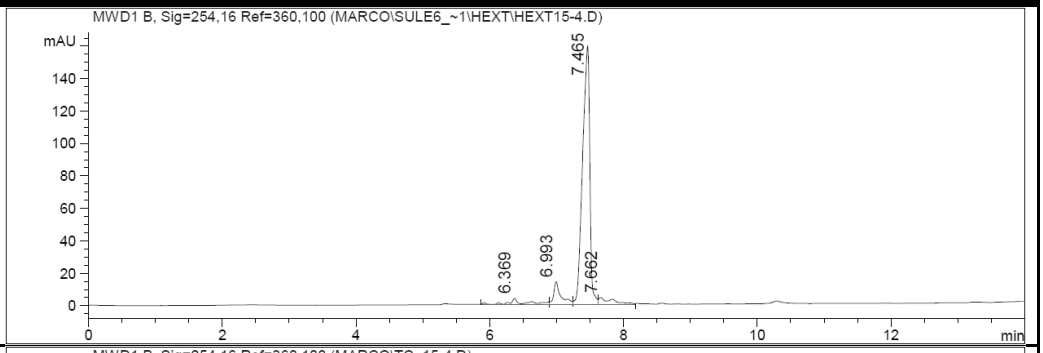
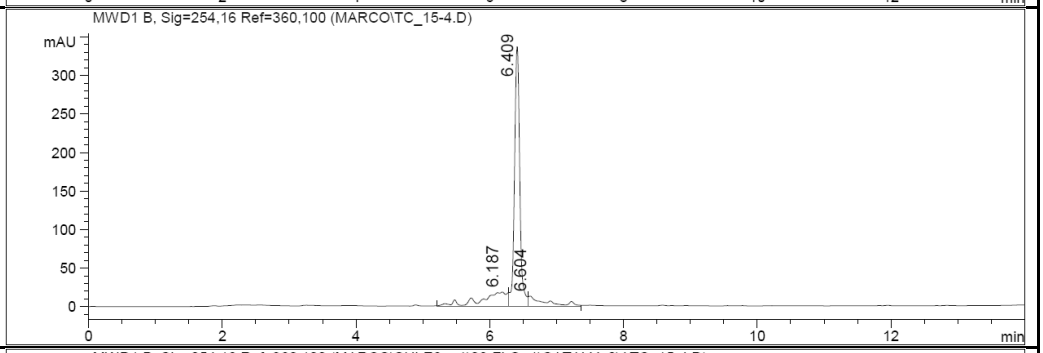
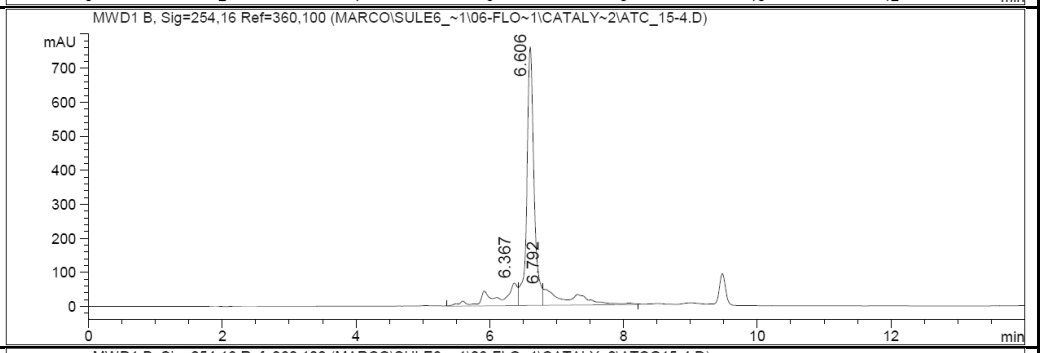
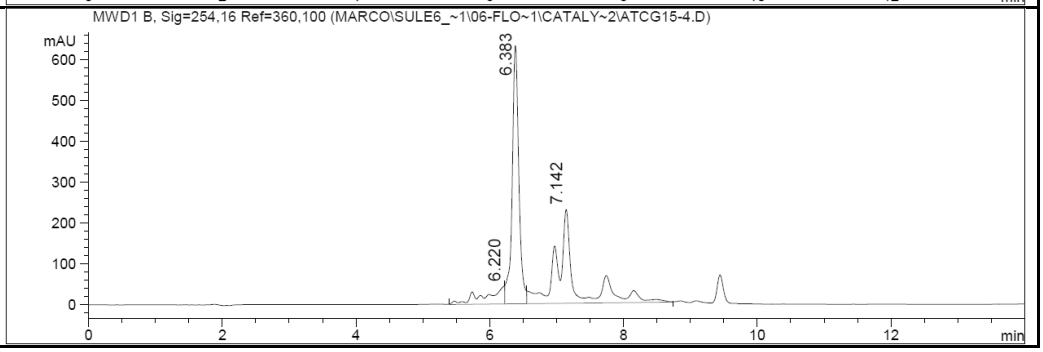
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $RuCl_3$ (200 equiv., 4 µmol) in dry ACN.

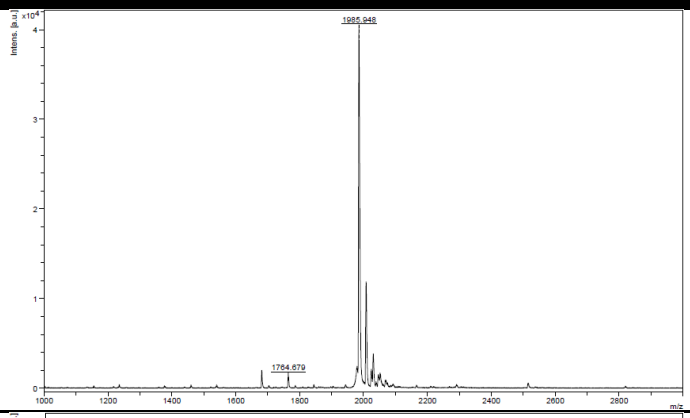
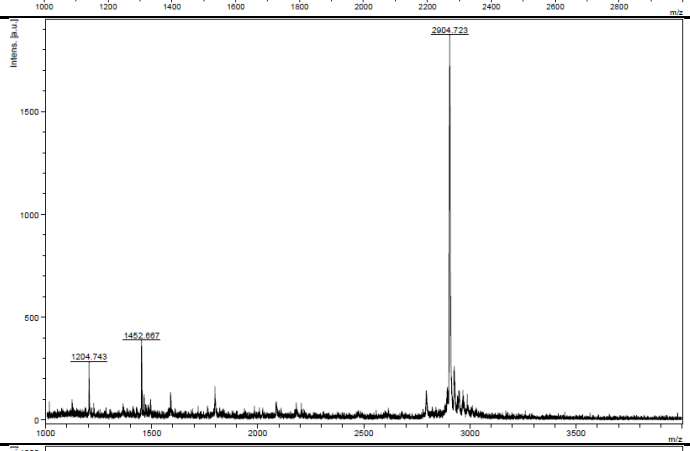
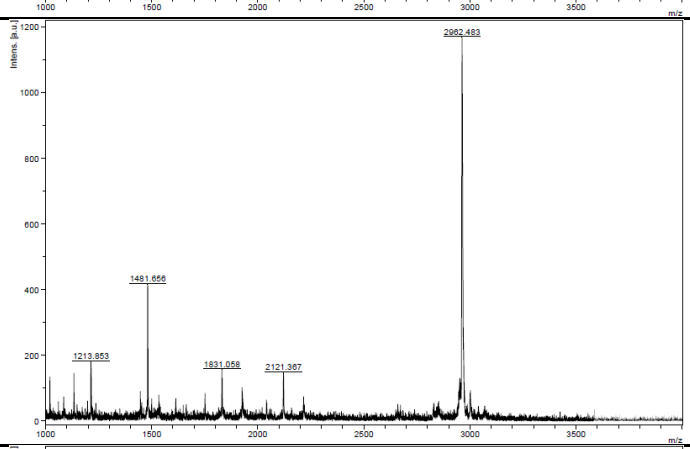
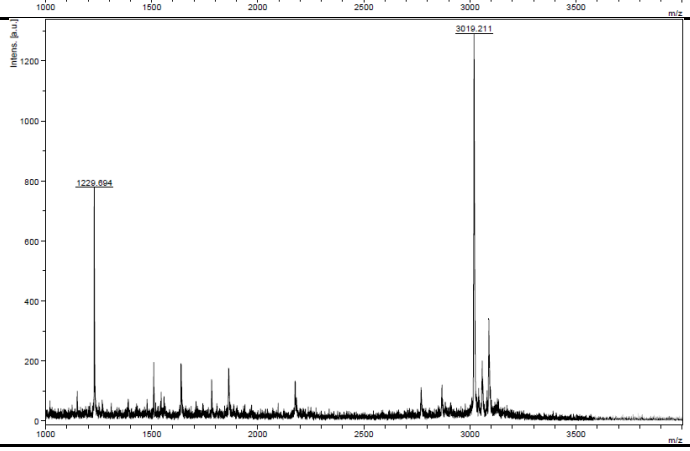
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.1
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2906.2
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.6
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3021.6

CPG-oligonucleotide + [Ru(*p*-cymene)Cl_2]$_2$

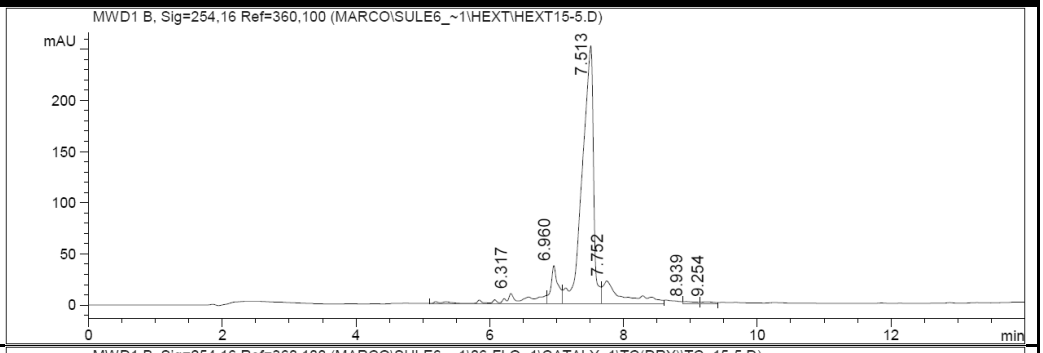
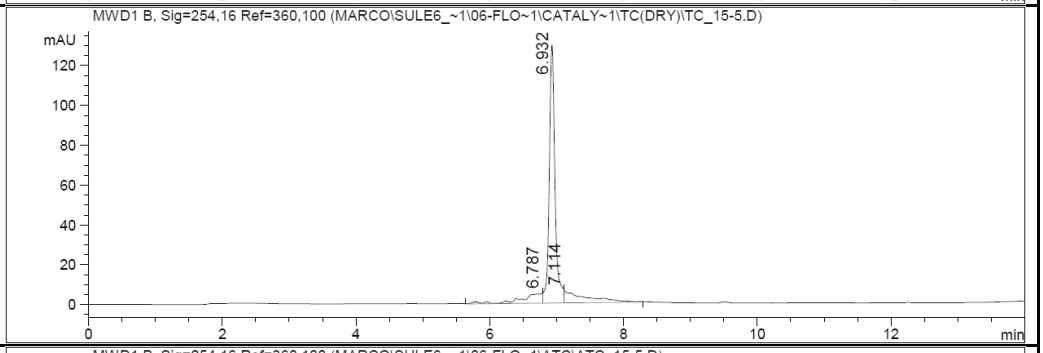
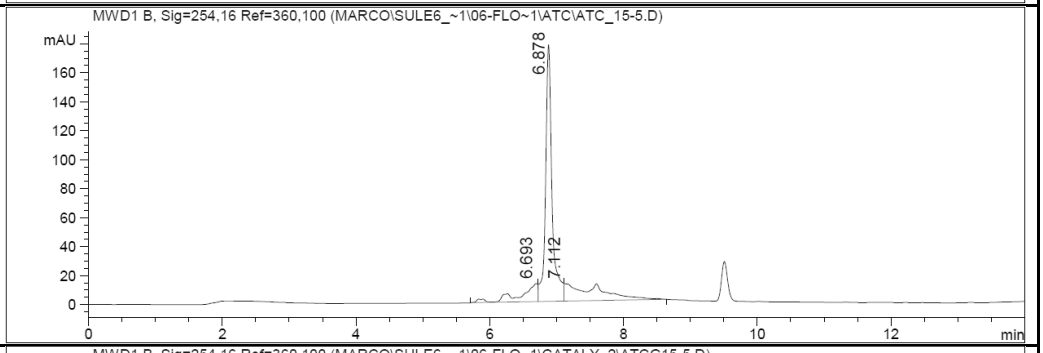
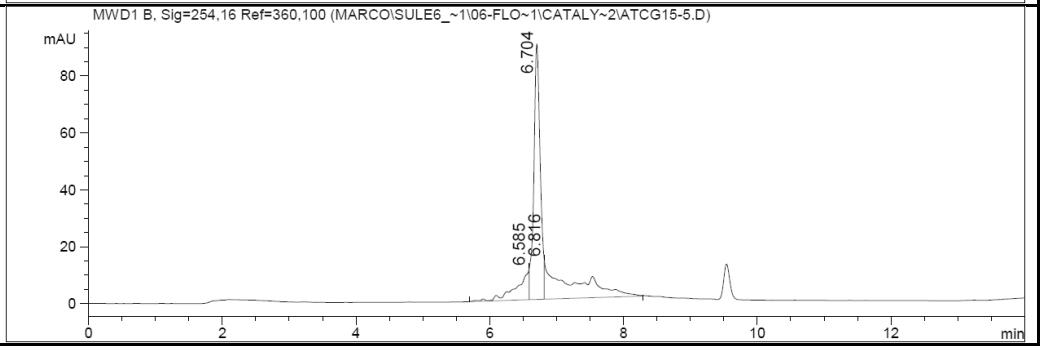
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with [Ru(*p*-cymene)Cl_2]$_2$ (200 equiv., 4 µmol) in dry CH_2Cl_2.

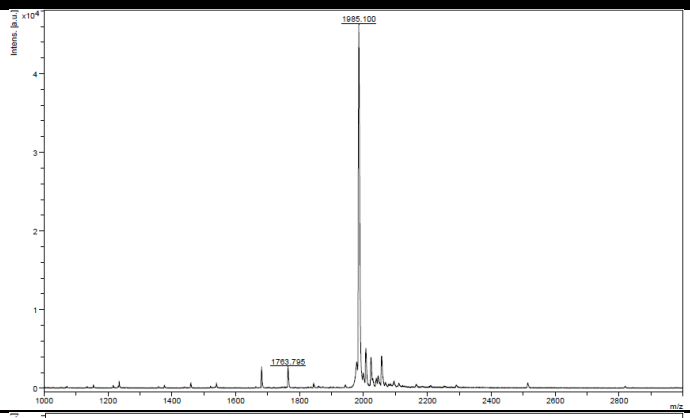
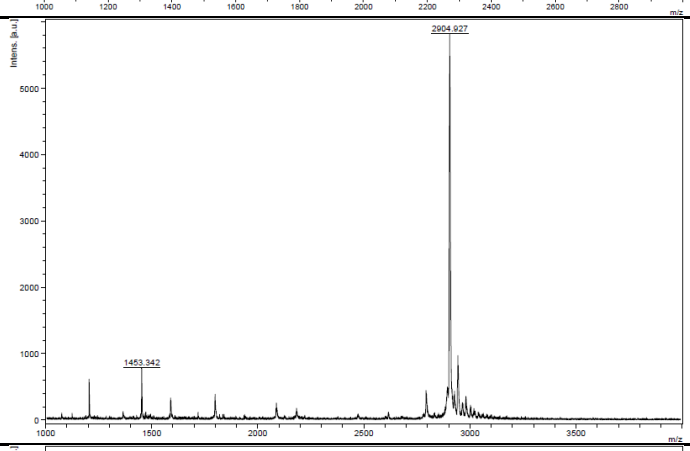
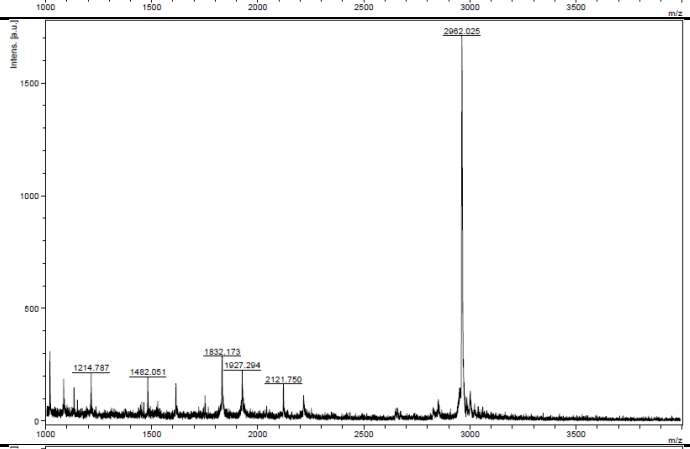
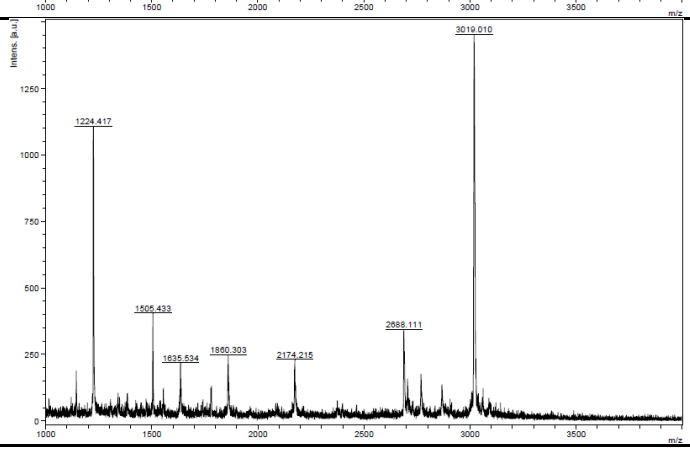
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.5
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.2

CPG-oligonucleotide + Ru(Me-allyl)$_2$(cod)

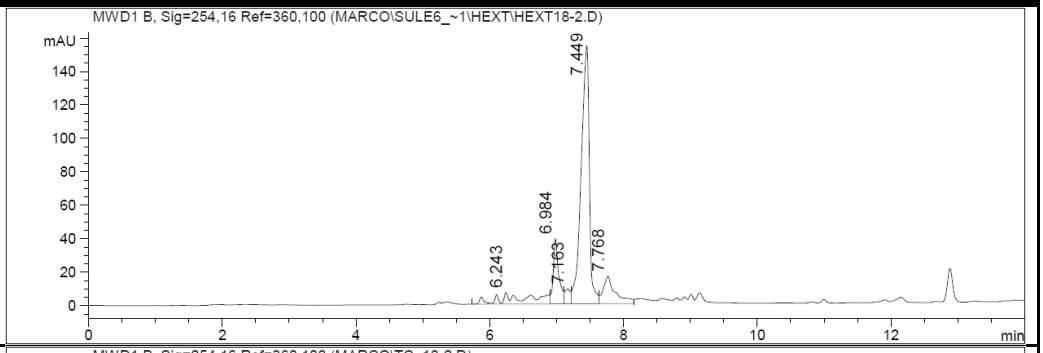
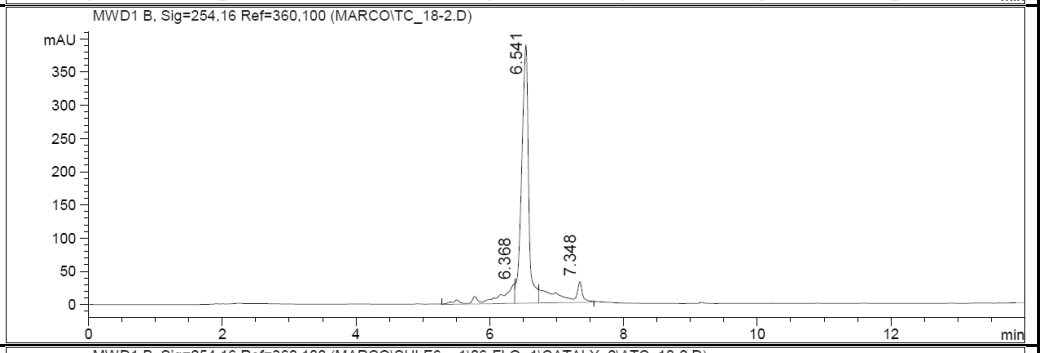
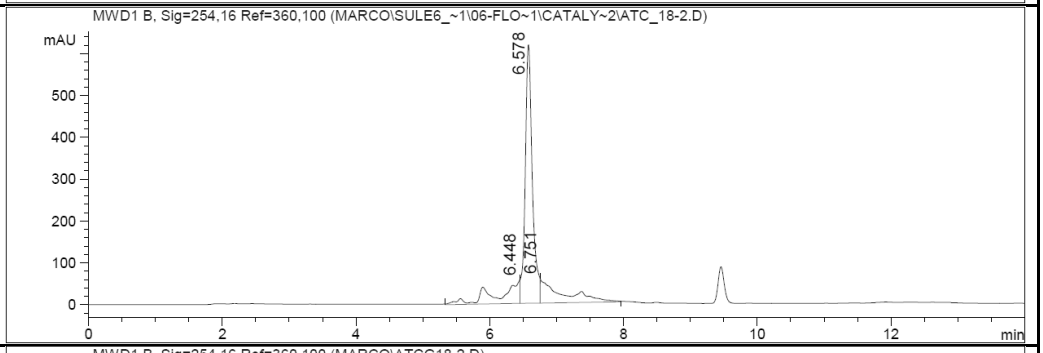
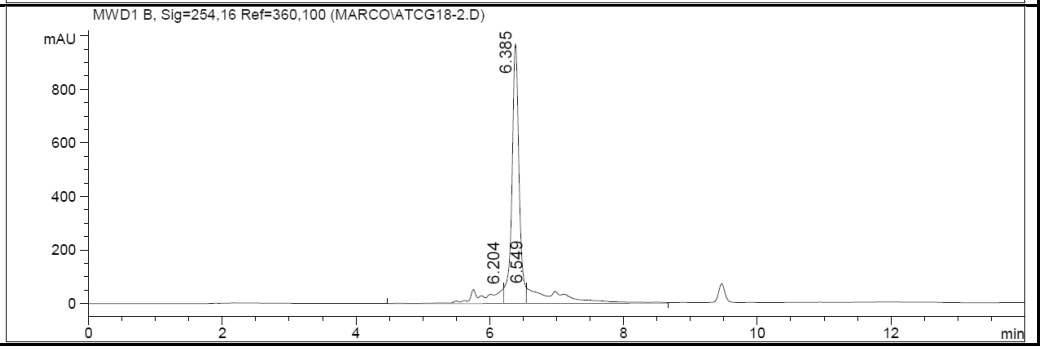
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with Ru(Me-allyl)$_2$(cod) (200 equiv., 4 µmol) in dry CH_2Cl_2.

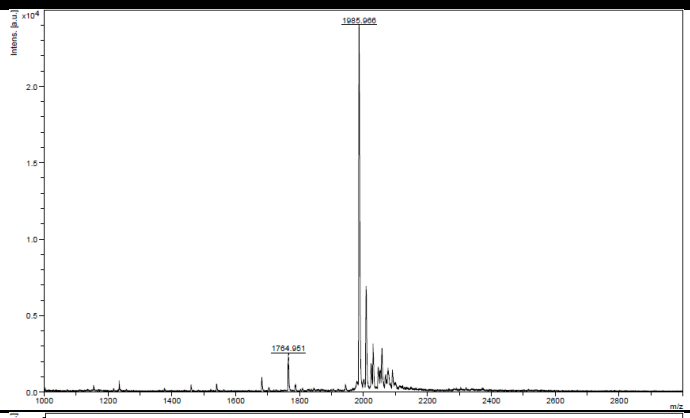
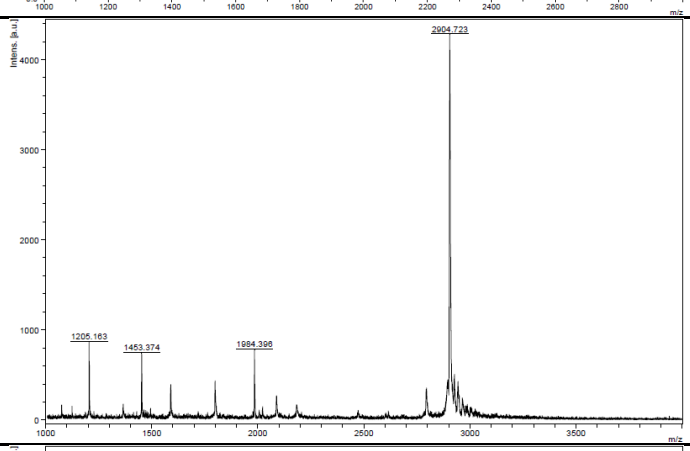
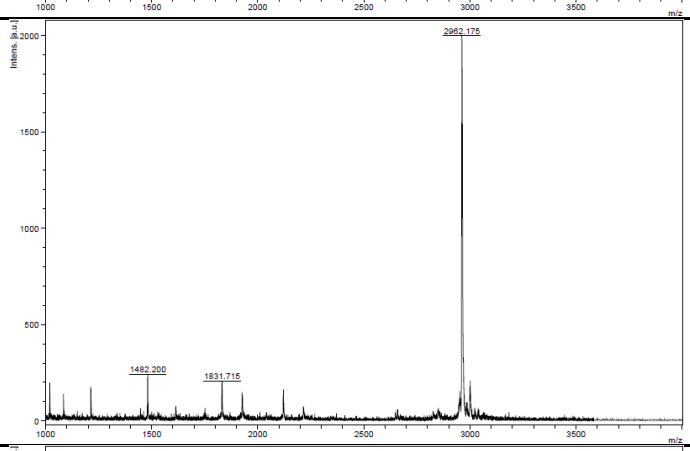
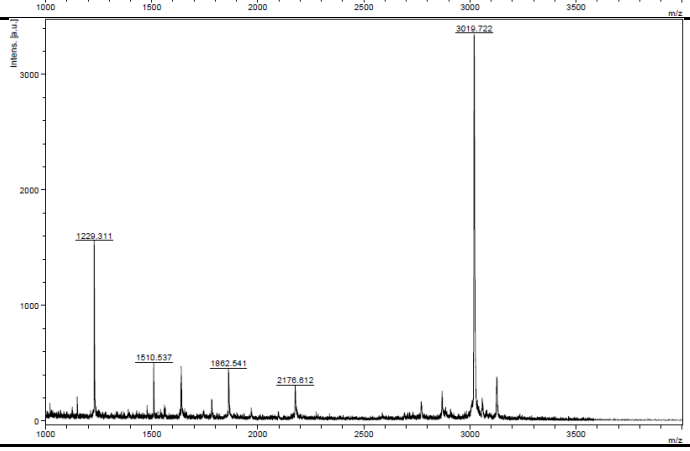
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.1
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.0

CPG-oligonucleotide + Grubbs 1st Gen.

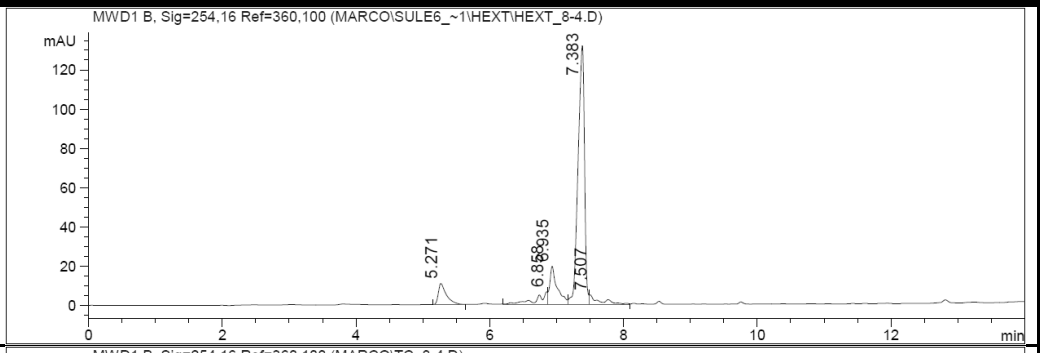
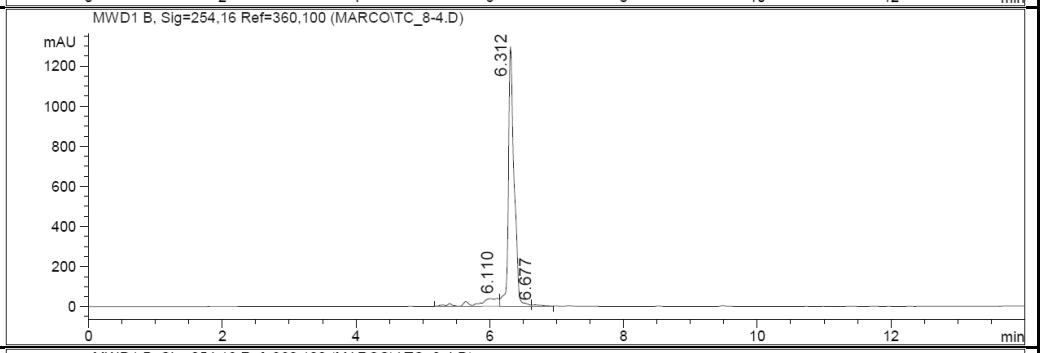
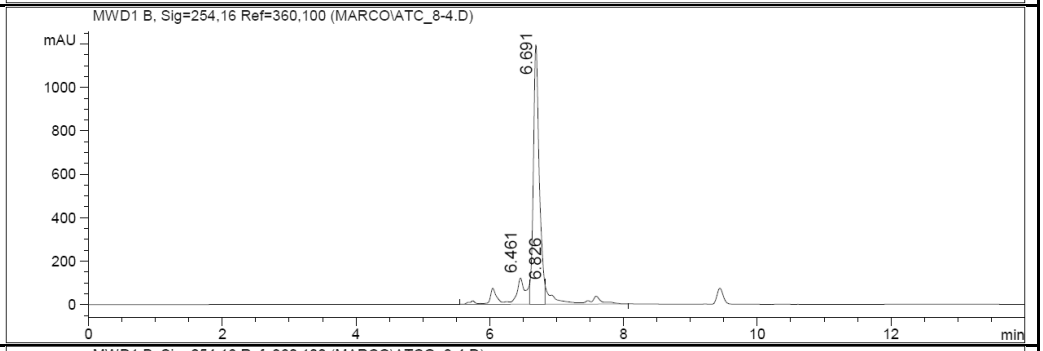
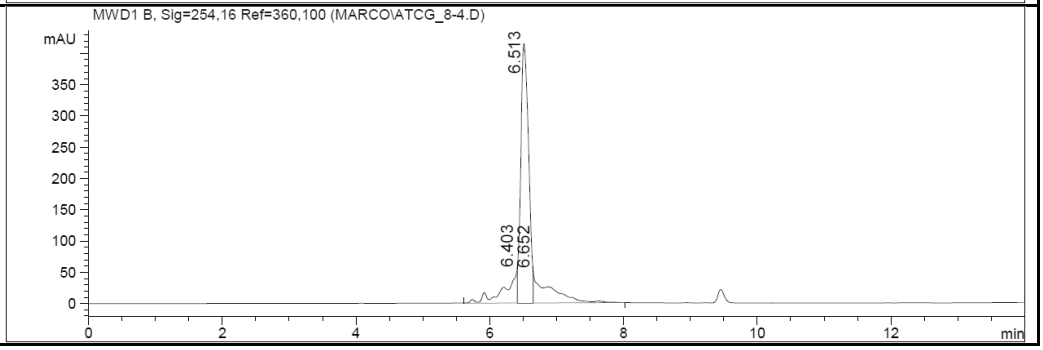
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with Grubbs 1st Gen. (200 equiv., 4 µmol) in dry CH_2Cl_2.

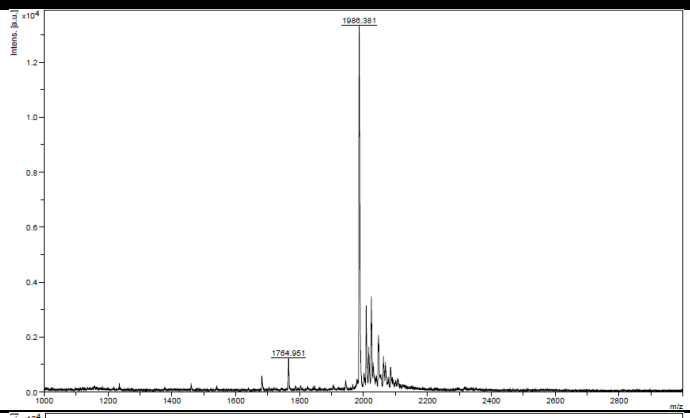
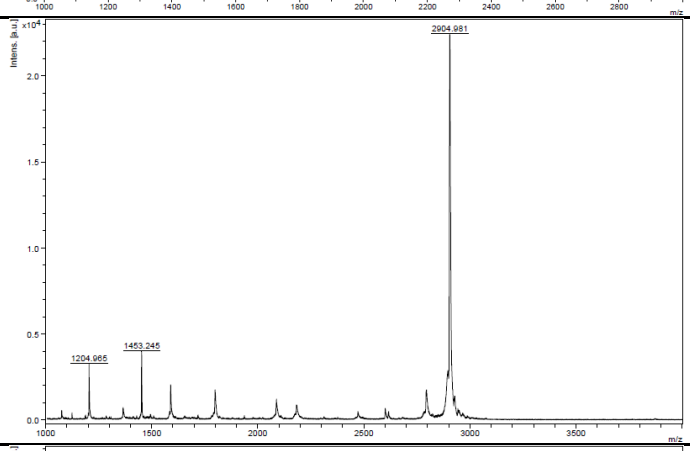
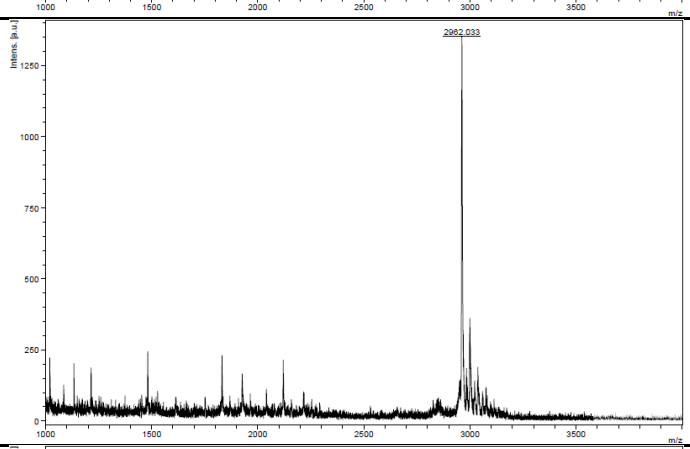
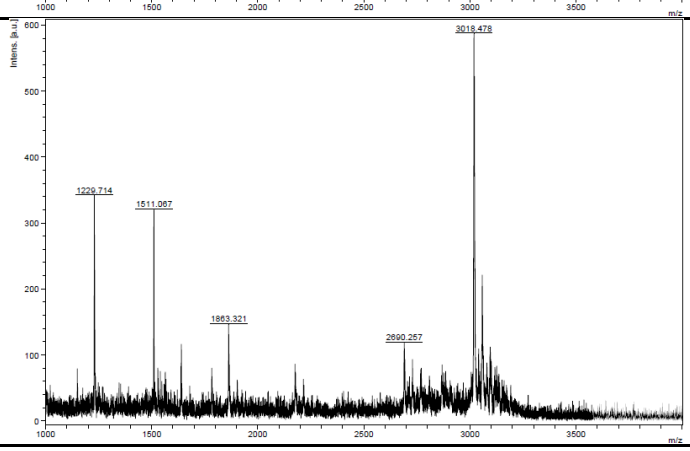
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.2
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.7

CPG-oligonucleotide + $SbCl_3$

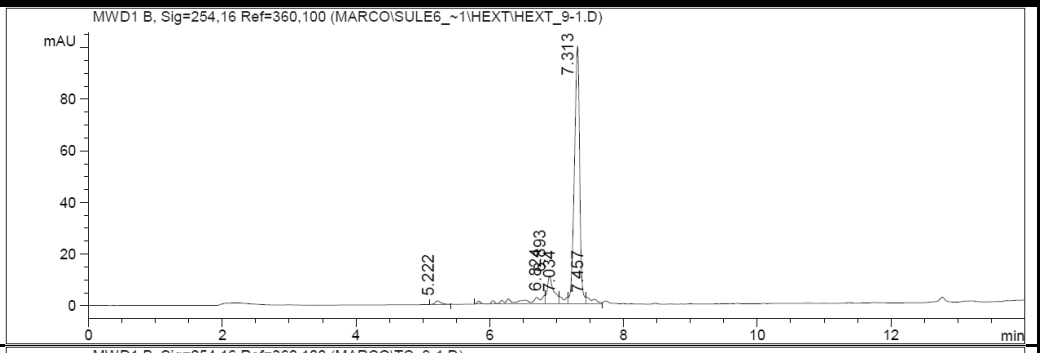
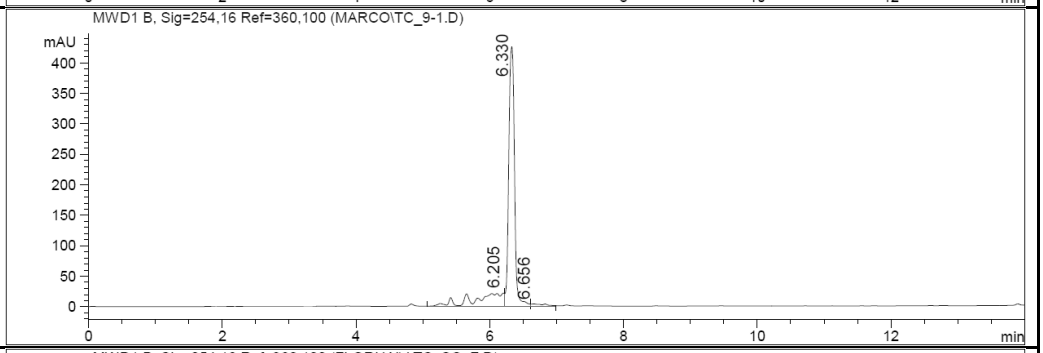
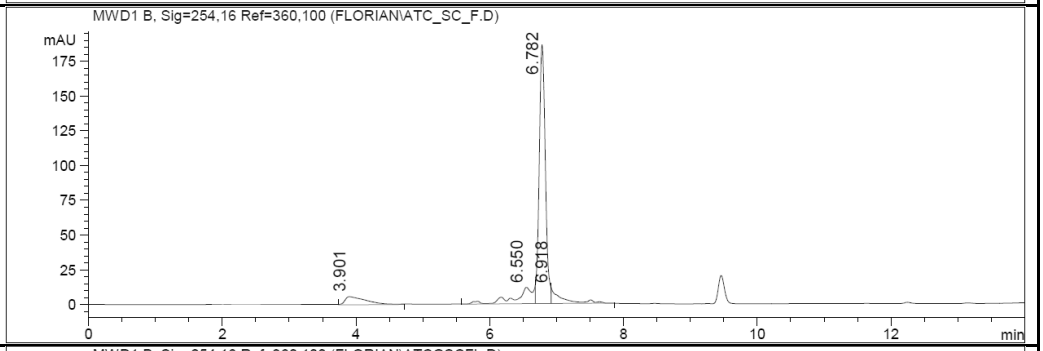
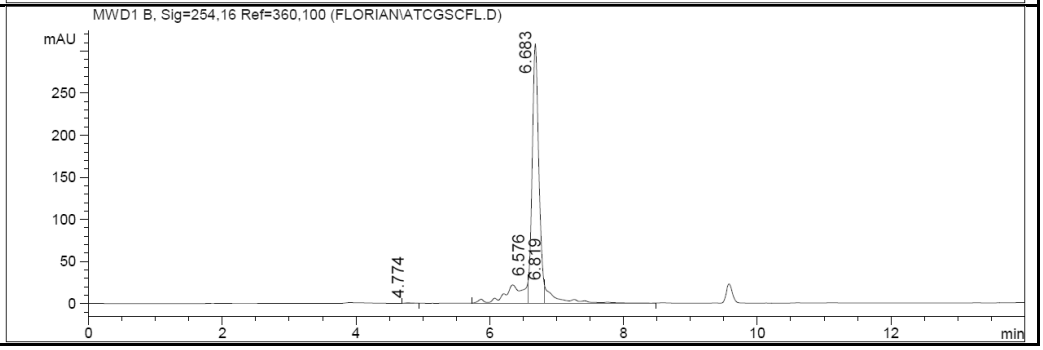
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $SbCl_3$ (200 equiv., 4 µmol) in dry ACN.

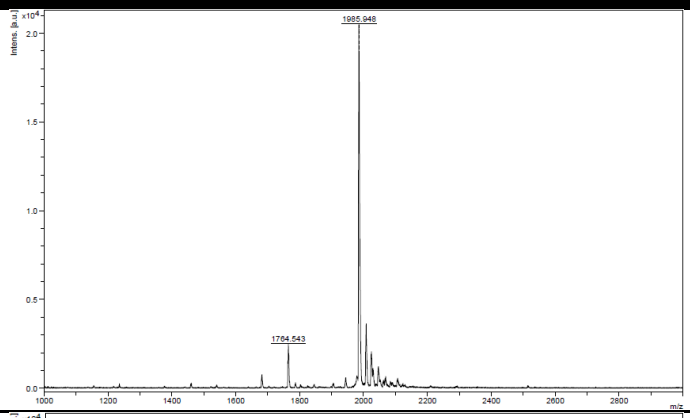
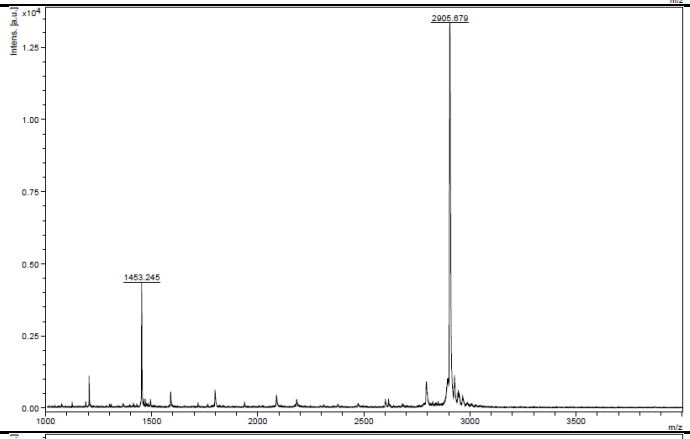
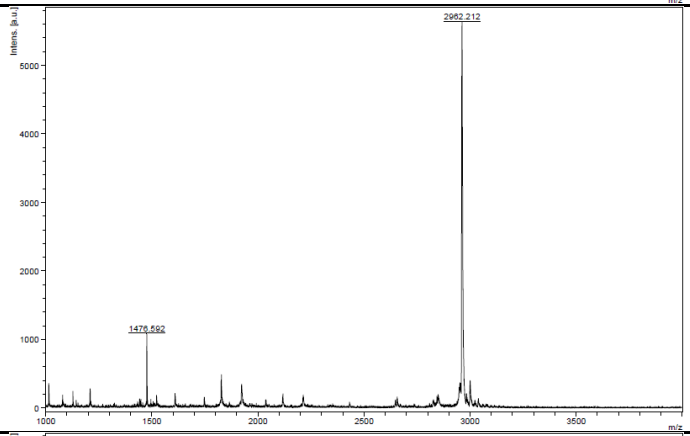
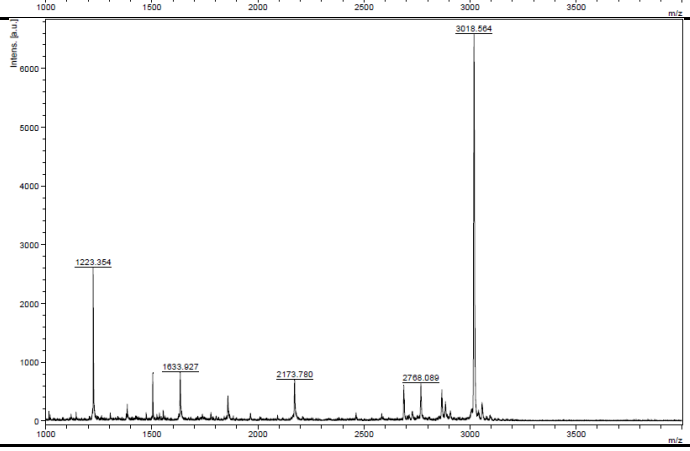
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.4
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.0
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.5

CPG-oligonucleotide + $Sc(OTf)_3$

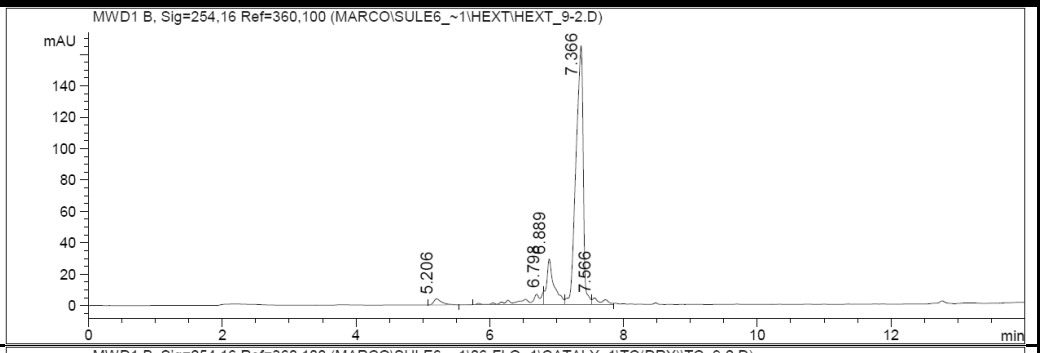
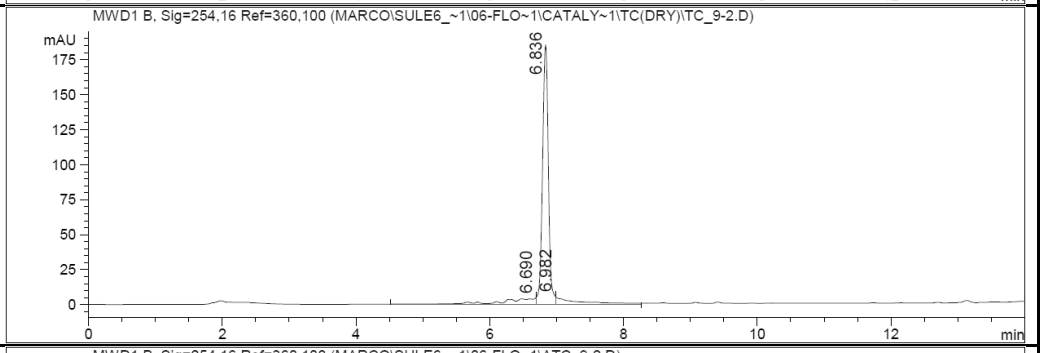
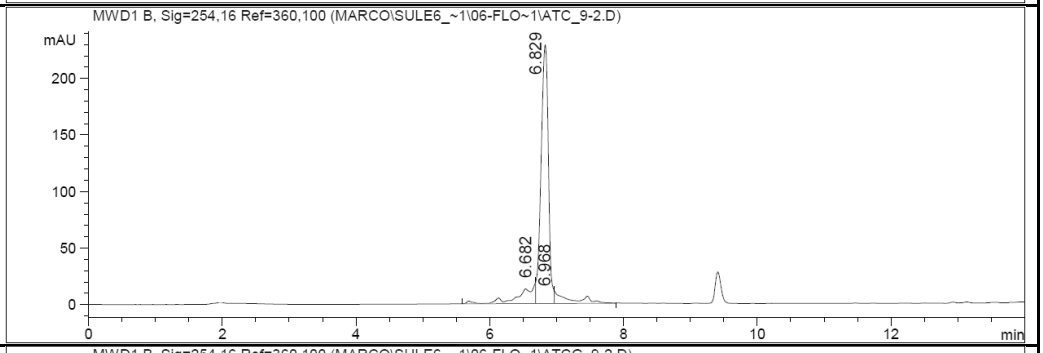
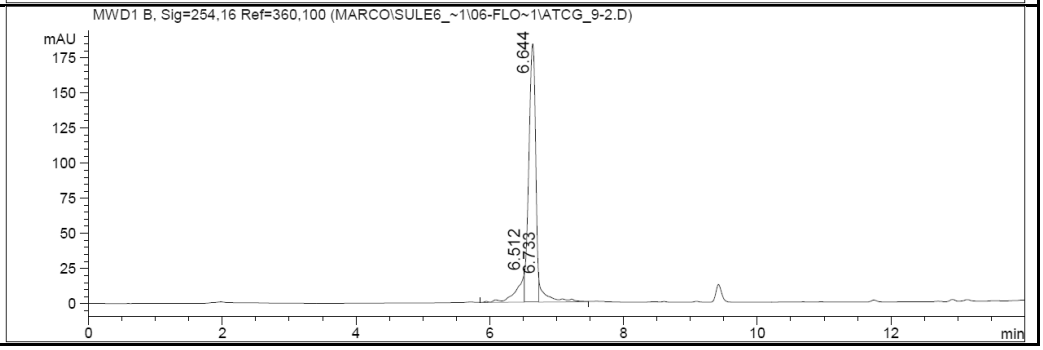
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Sc(OTf)_3$ (200 equiv., 4 µmol) in dry ACN.

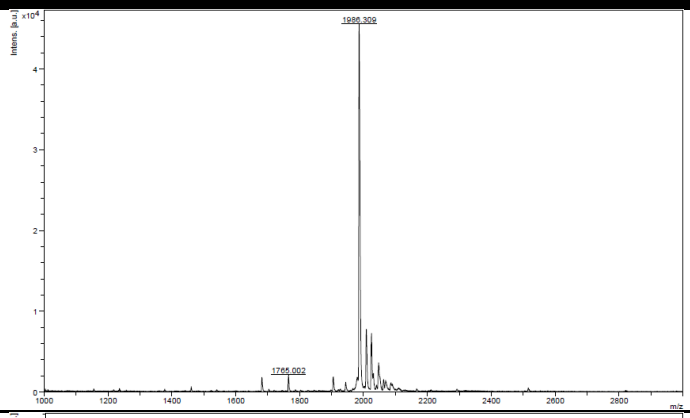
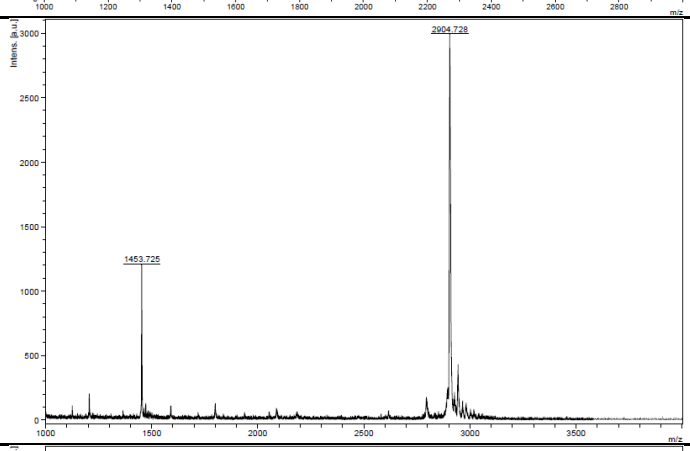
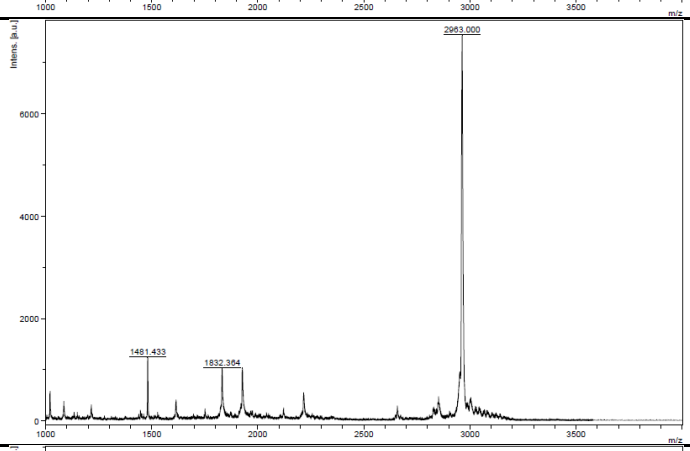
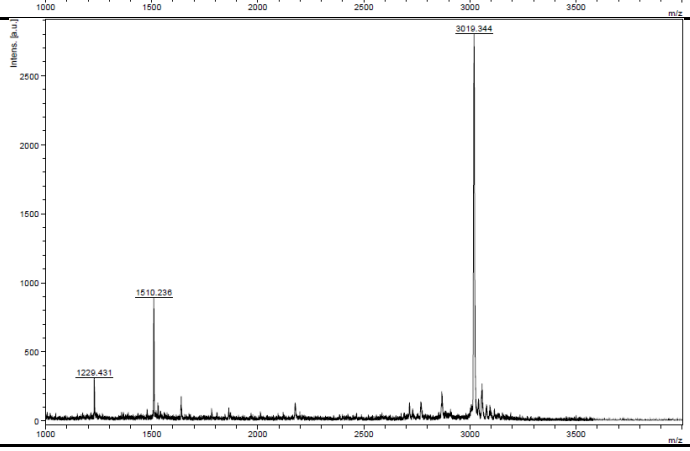
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.2
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

CPG-oligonucleotide + SeO_2

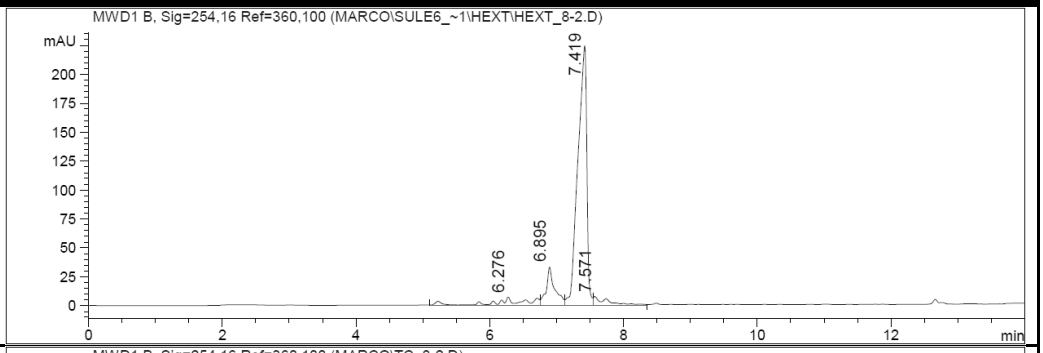
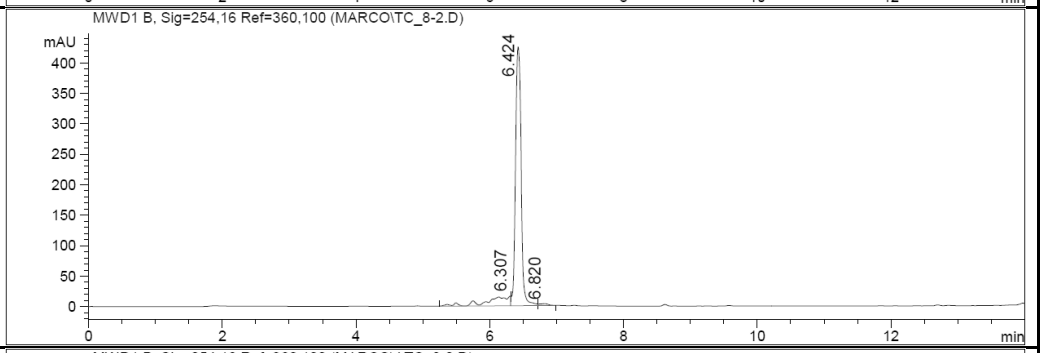
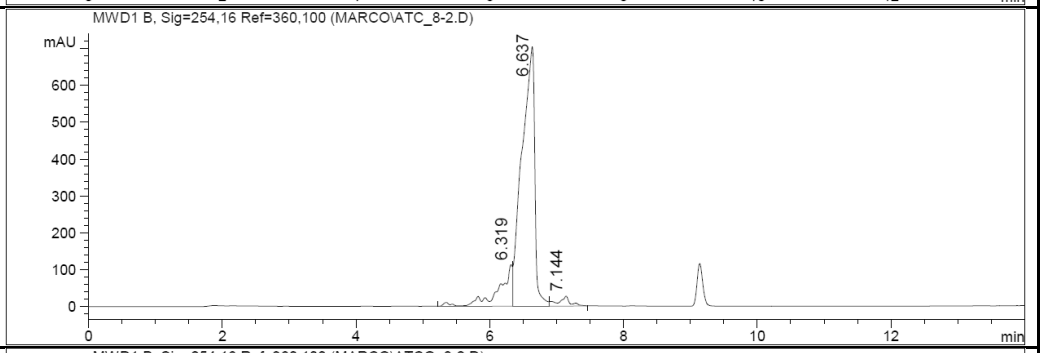
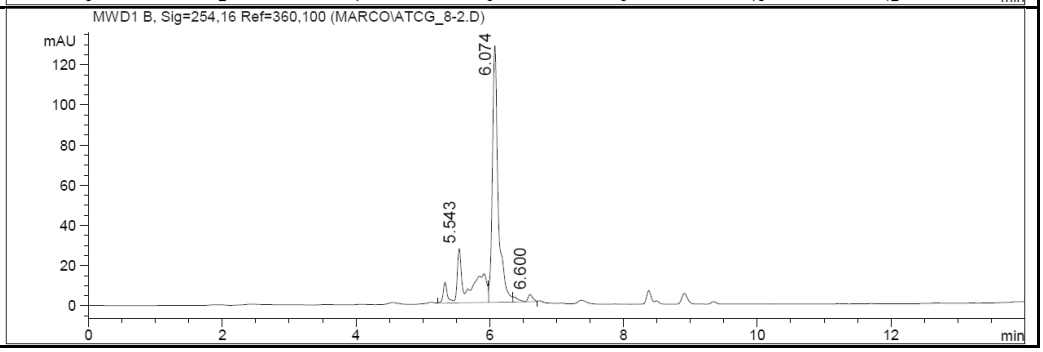
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with SeO_2 (200 equiv., 4 µmol) in dry MeOH.

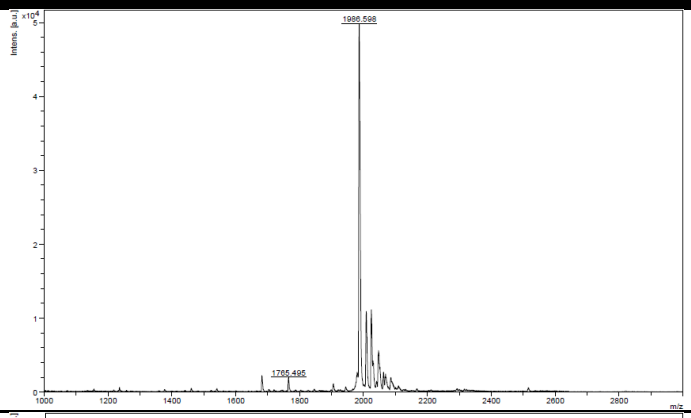
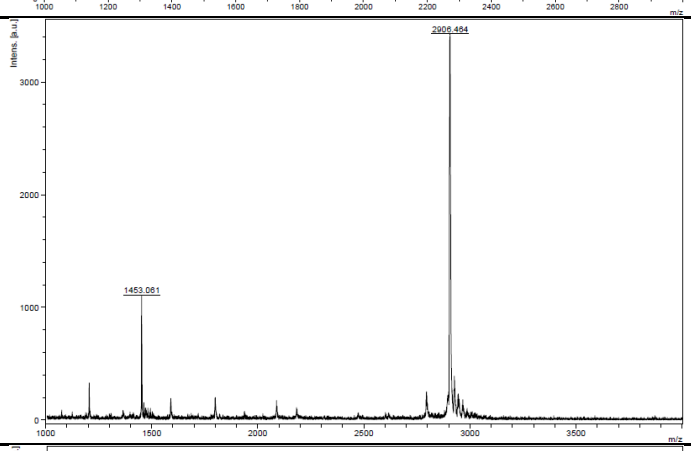
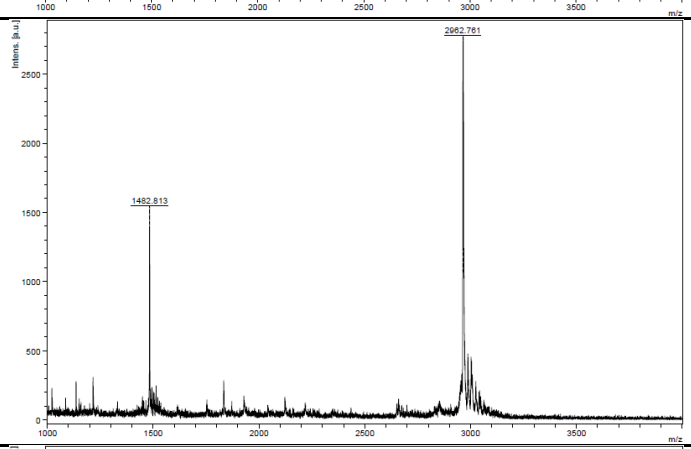
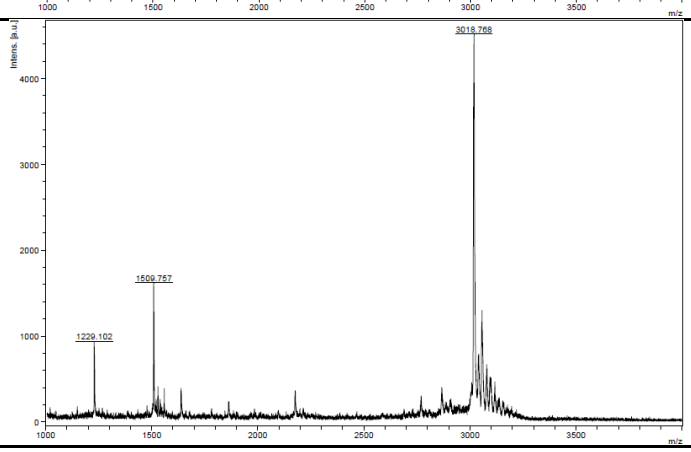
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.3

CPG-oligonucleotide + Ti(O*i*-Pr)$_4$

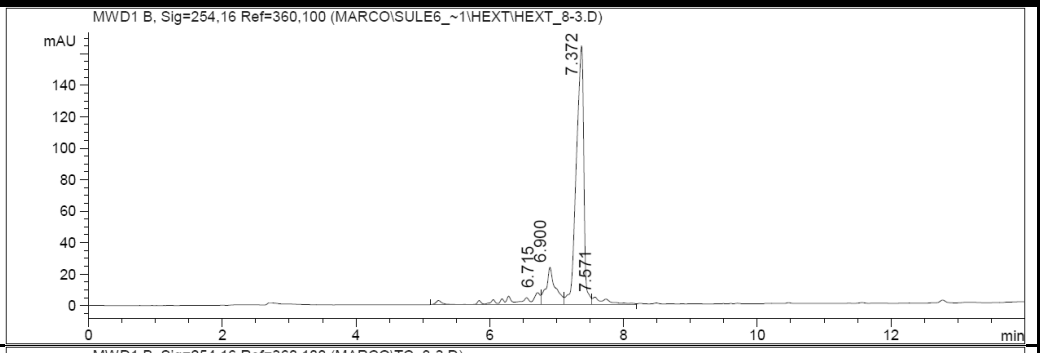
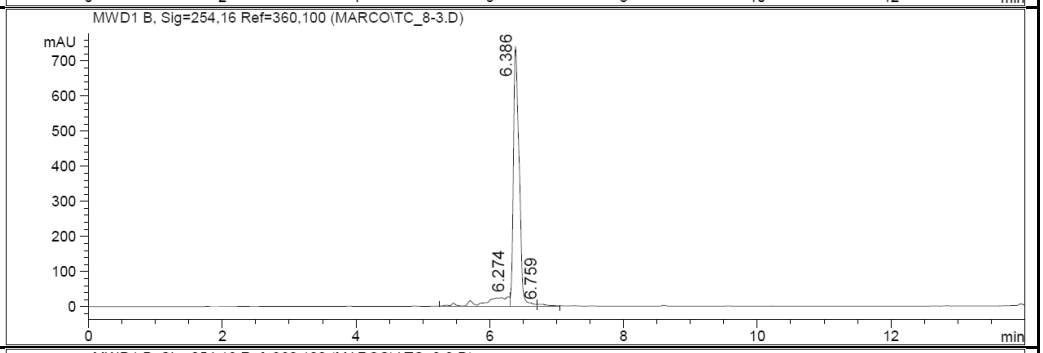
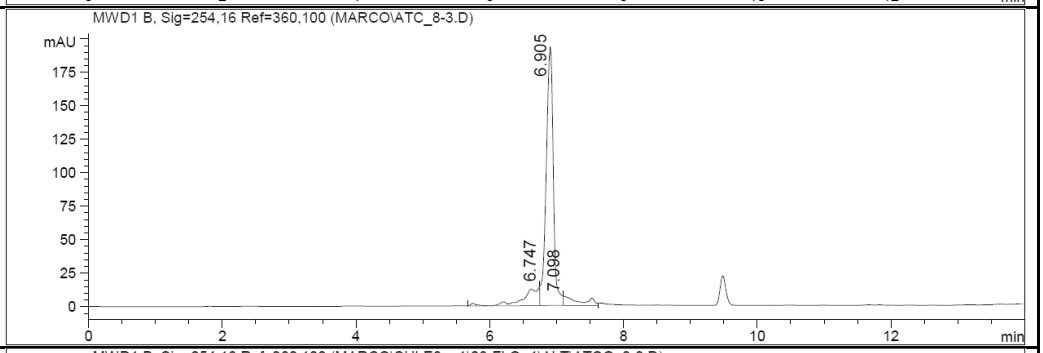
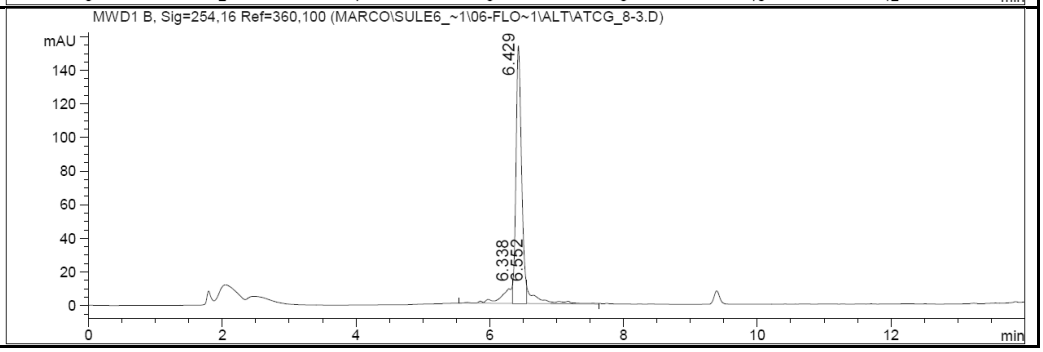
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with Ti(O*i*-Pr)$_4$ (200 equiv., 4 µmol) in dry MeOH.

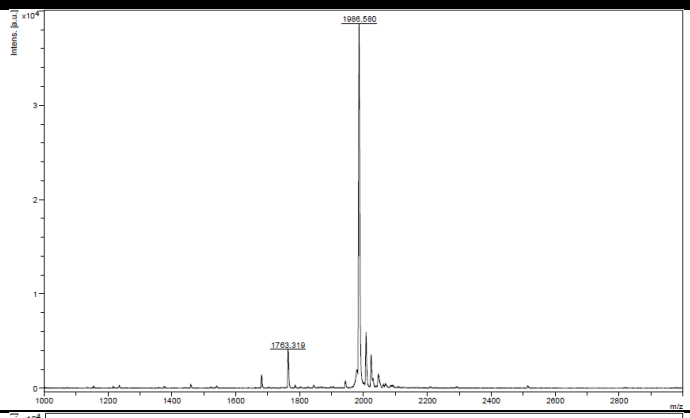
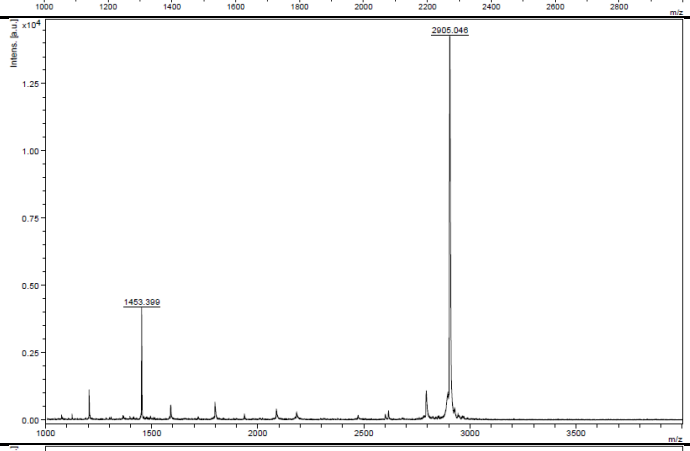
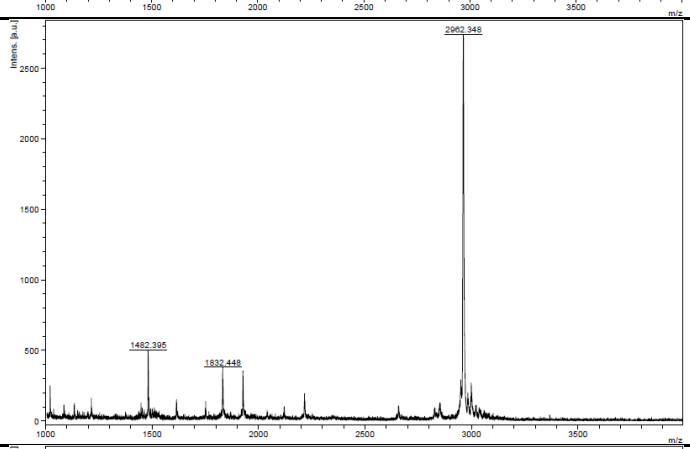
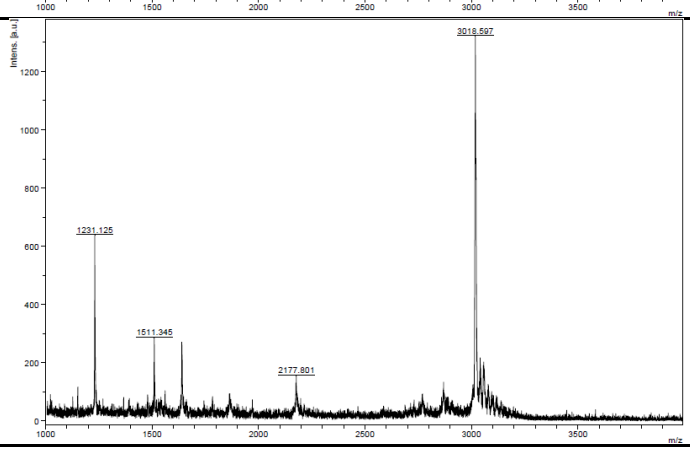
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2906.5
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.8

CPG-oligonucleotide + $VO(acac)_2$

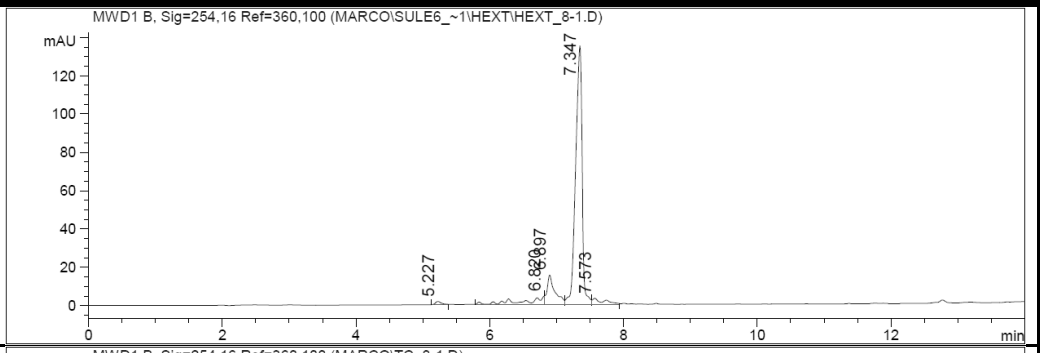
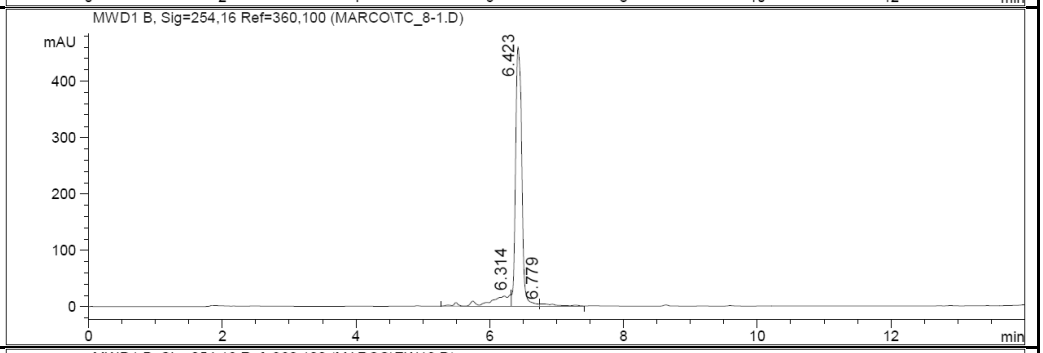
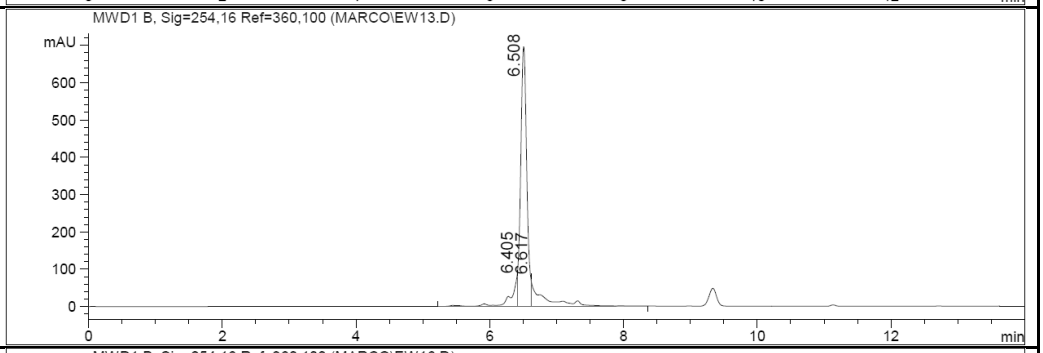
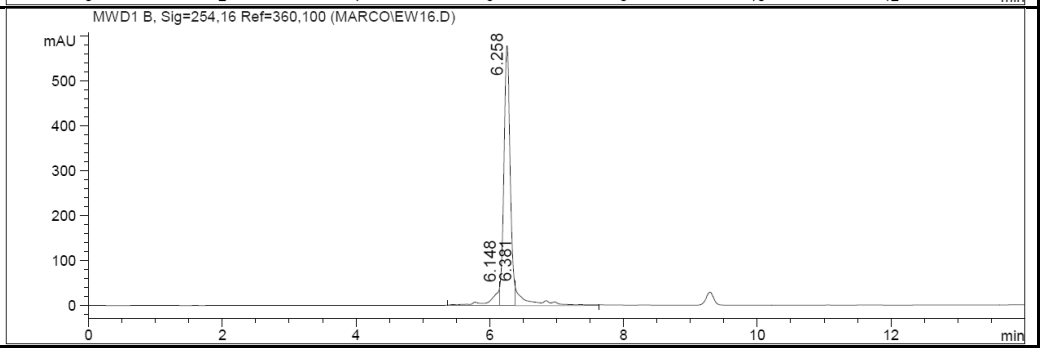
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $VO(acac)_2$ (200 equiv., 4 µmol) in dry MeOH.

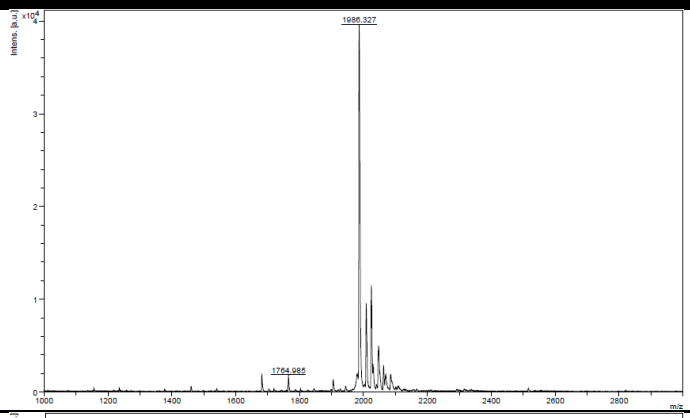
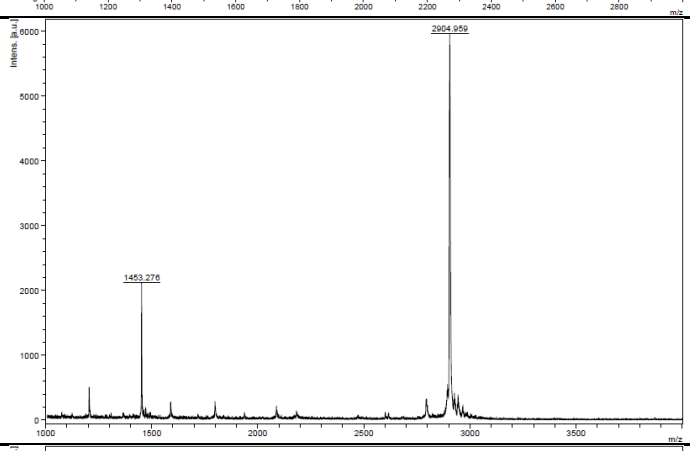
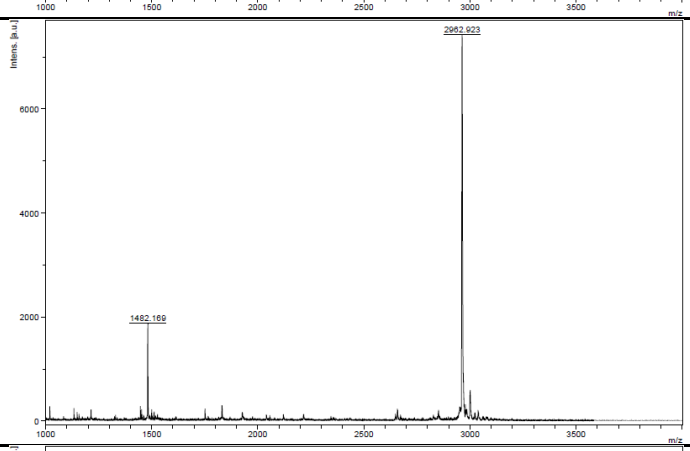
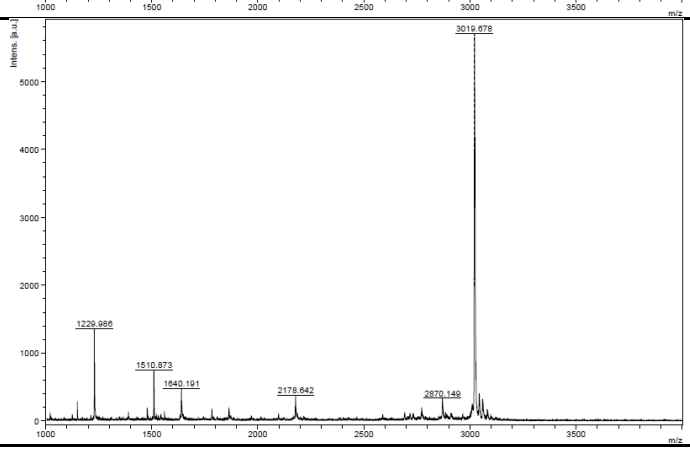
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.0
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

CPG-oligonucleotide + $Yb(OTf)_3$

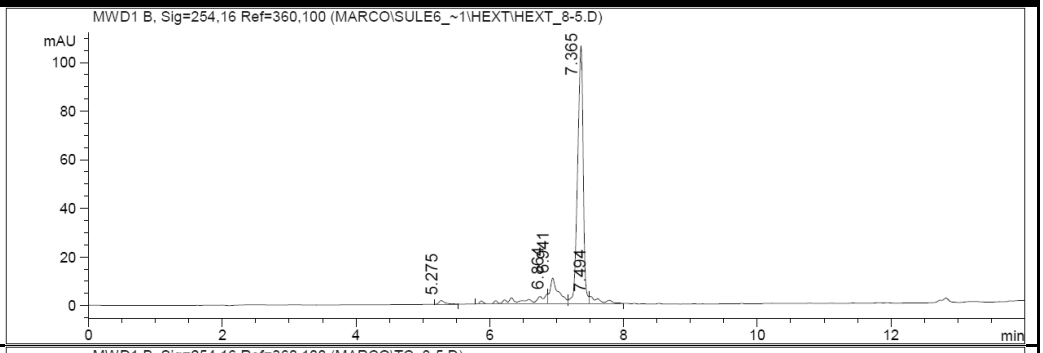
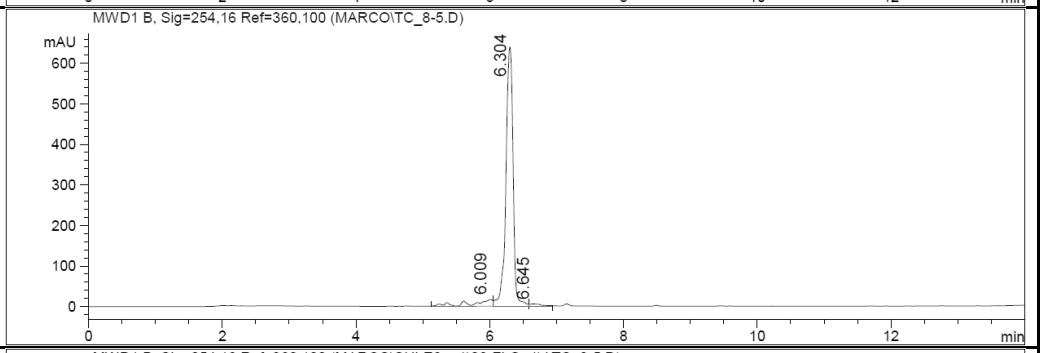
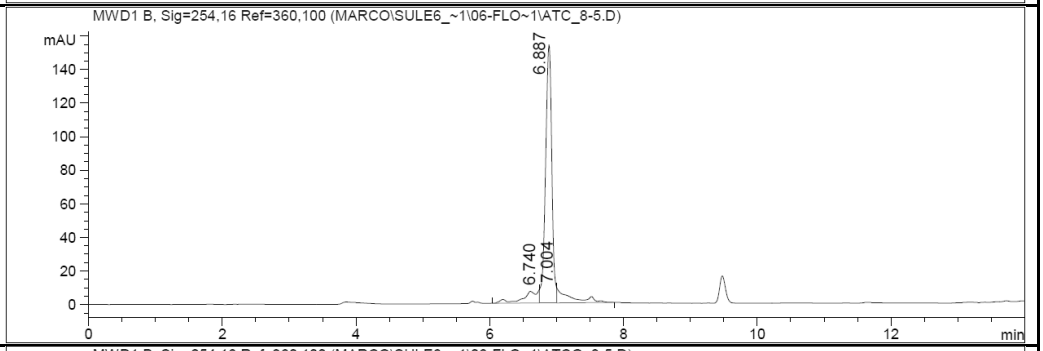
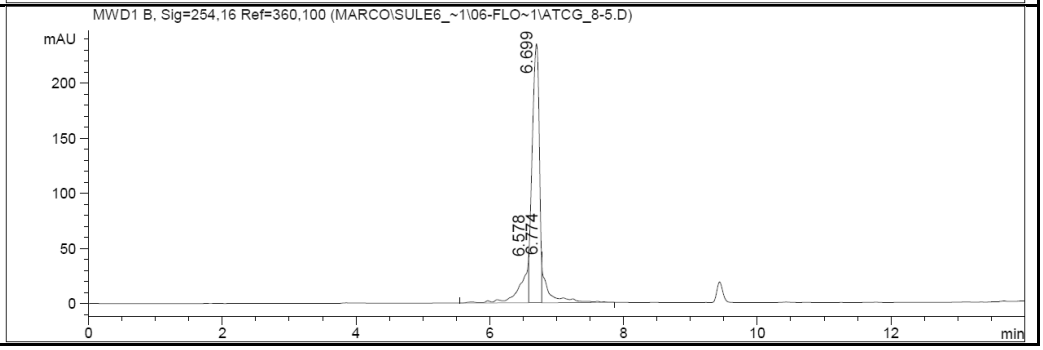
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Yb(OTf)_3$ (200 equiv., 4 µmol) in dry MeOH.

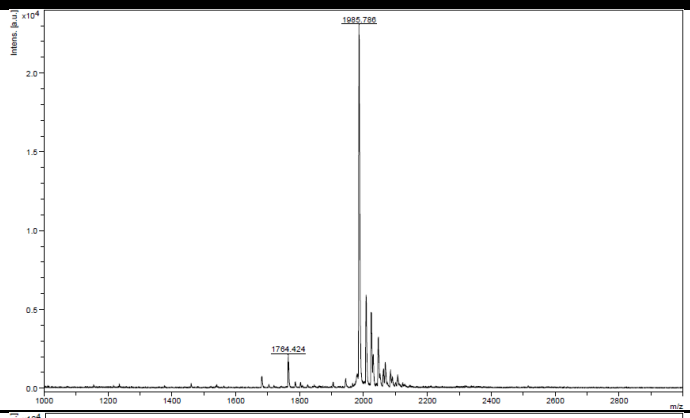
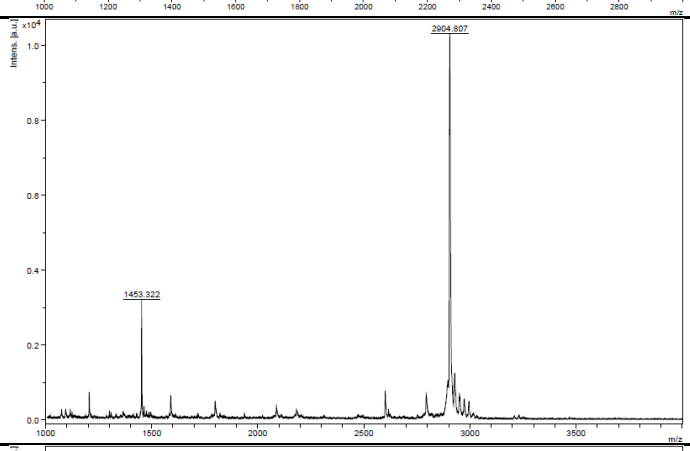
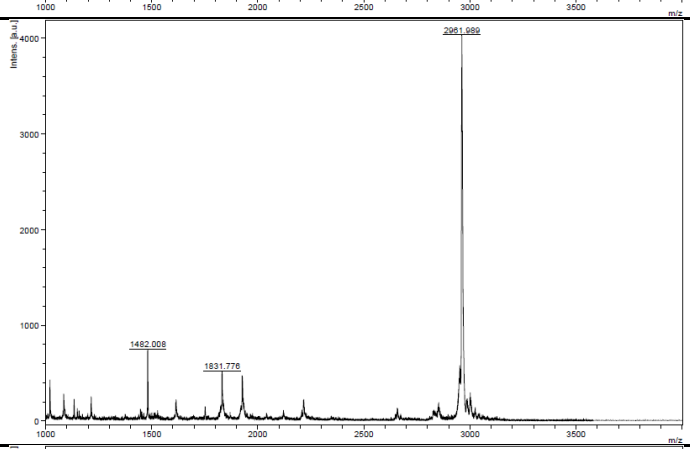
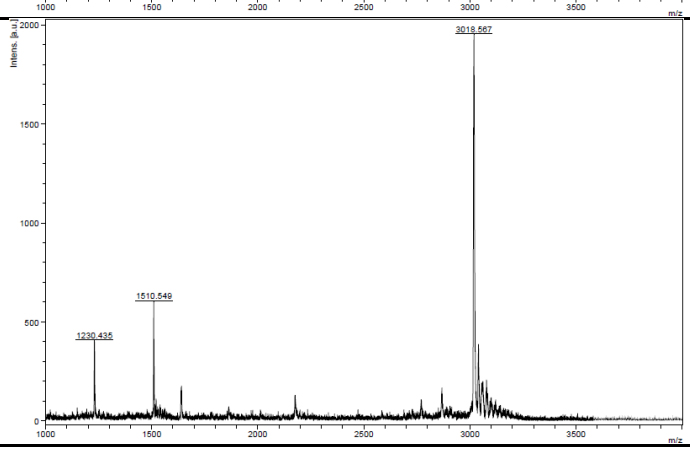
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.0
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.7

CPG-oligonucleotide + $ZnCl_2$

According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $ZnCl_2$ (200 equiv., 4 µmol) in dry ACN.

CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.8
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.8
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

TableS2 – Stability of DNA against metal salts at 40 °C[a]

Entry	Metal salt	Solvent	ATC	ATCG
1	$Cu(OTf)_2$	ACN		
2	$InCl_3$	ACN		
3	SeO_2	MeOH		
4	$Yb(OTf)_3$	MeOH		
5	$Sc(OTf)_3$	ACN		

[a] for each: 20 nmol DNA, 200 eq. transition metal salt, 50 µL solvent (HPLC-grade), 40 °C., 22 h. ACN = acetonitrile, MeOH = methanol.

Table S3 – Stability of DNA against metal salts dissolved in benchtop solvents[a]

Entry	Metal salt	Solvent	ATC	ATCG
1	AgOTf	ACN		
2	$BiBr_3$	ACN		
3	$InCl_3$	ACN		
4	LiBr	ACN		
5	$Ni(acac)_2$	ACN		
6	$Yb(OTf)_3$	MeOH		

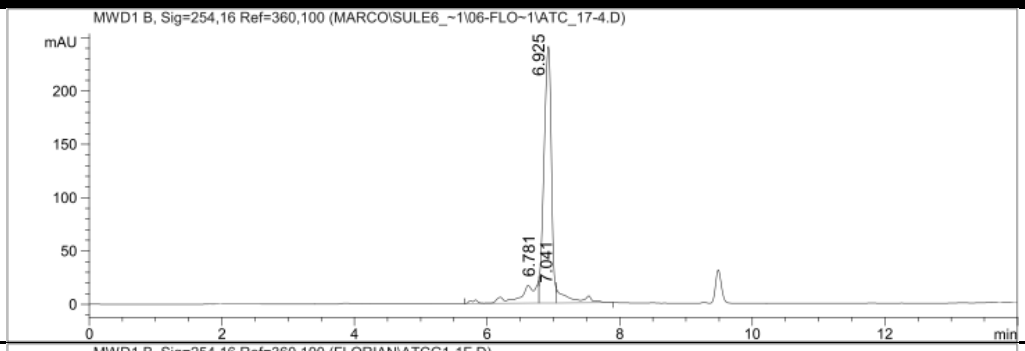
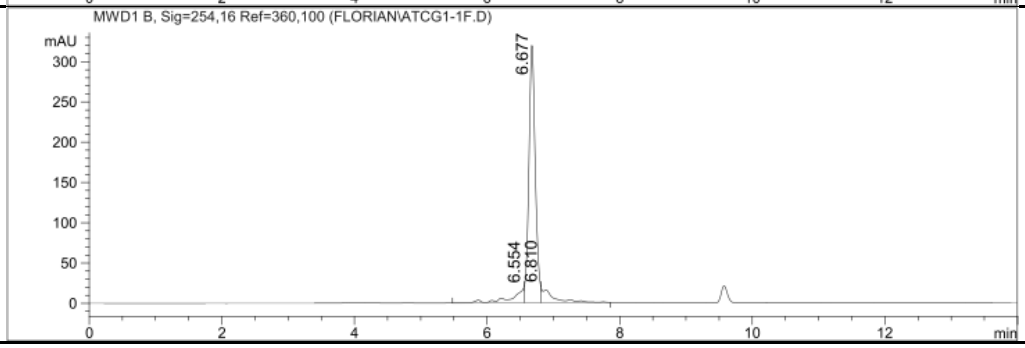
[a] for each: 20 nmol DNA, 200 eq. transition metal salt, 50 µL solvent (HPLC-grade), r.t., 22 h. ACN = acetonitrile, MeOH = methanol.

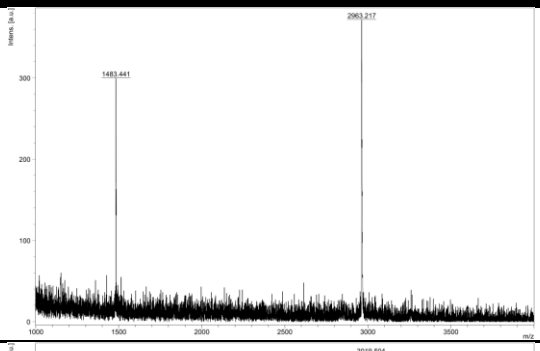
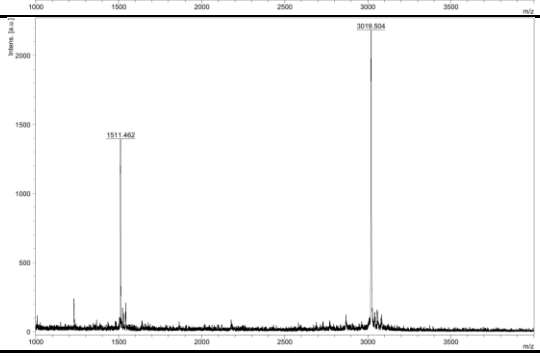
				DNA degradation
0-20%	21-40%	41-60%	> 61%	

HPLC traces and MALDI-MS spectra of metal ion screens

CPG-oligonucleotide + $Cu(OTf)_2$

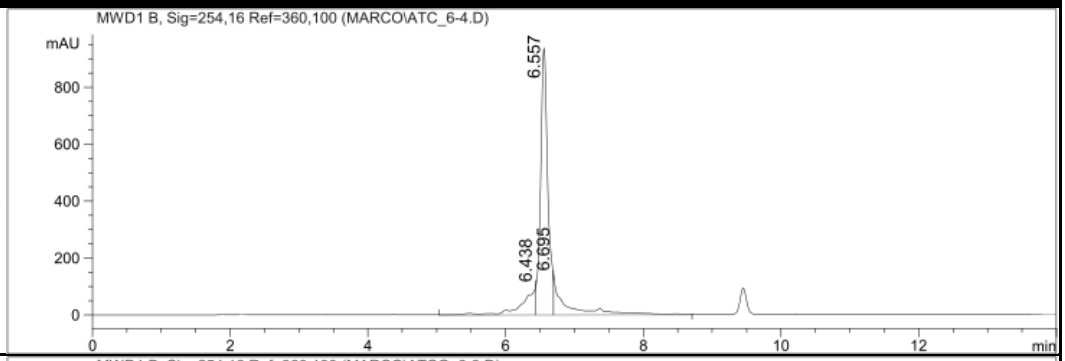
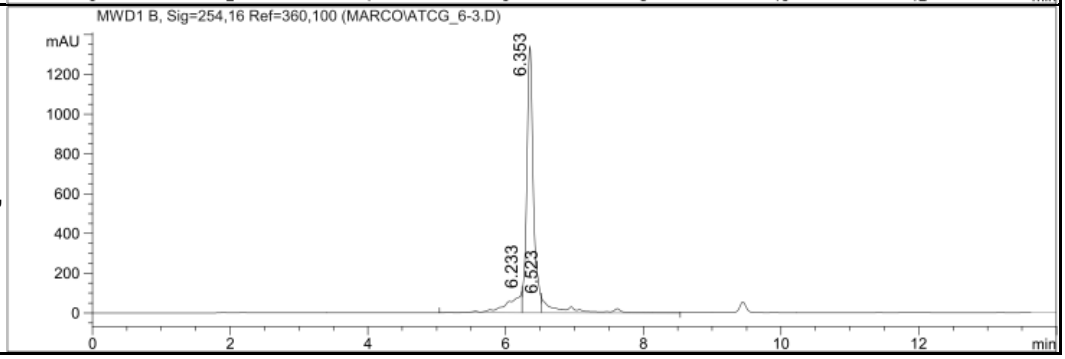
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Yb(OTf)_3$ (200 equiv., 4 µmol) in dry ACN at 40 °C.

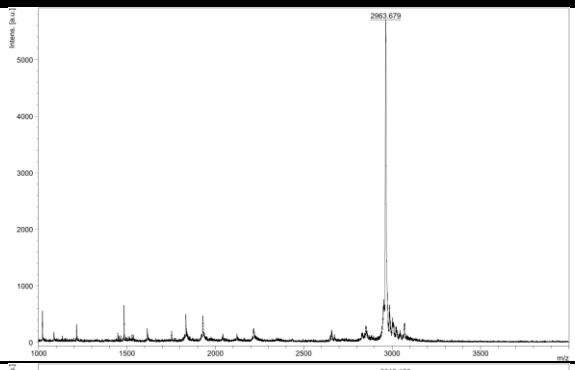
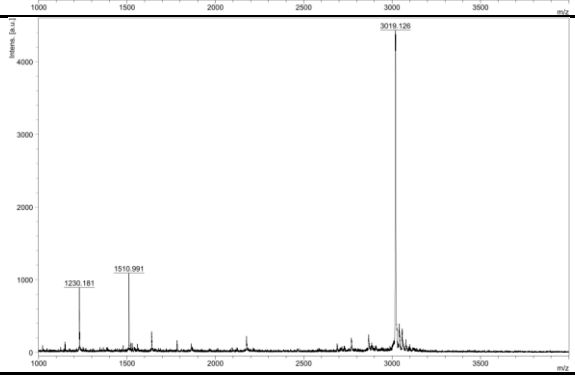
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.2
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.5

CPG-oligonucleotide + $InCl_3$

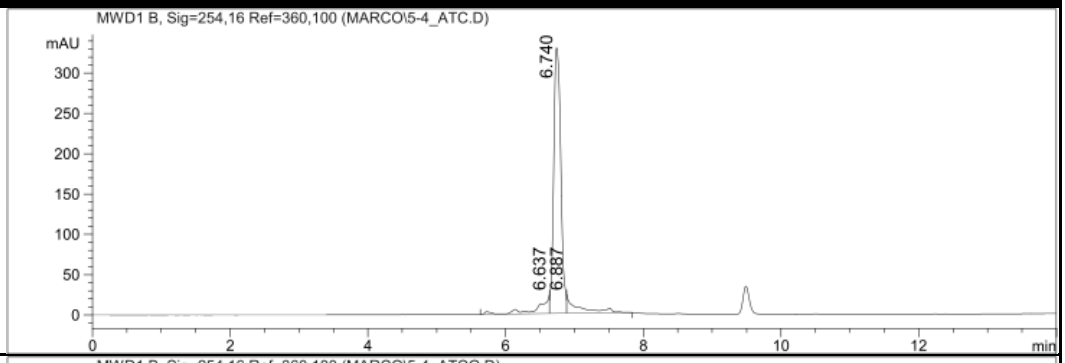
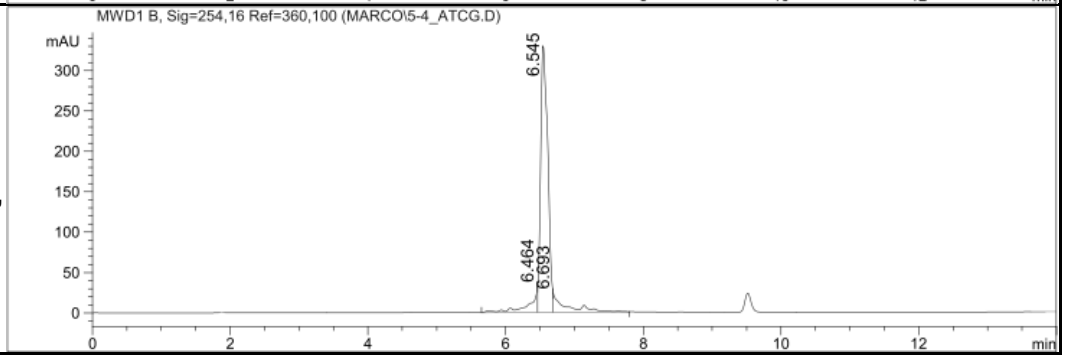
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $InCl_3$ (200 equiv., 4 µmol) in dry ACN at 40 °C.

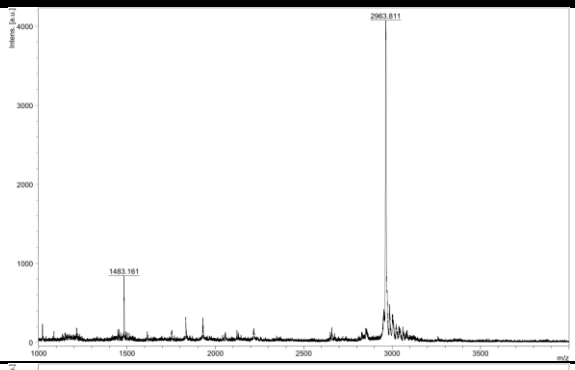
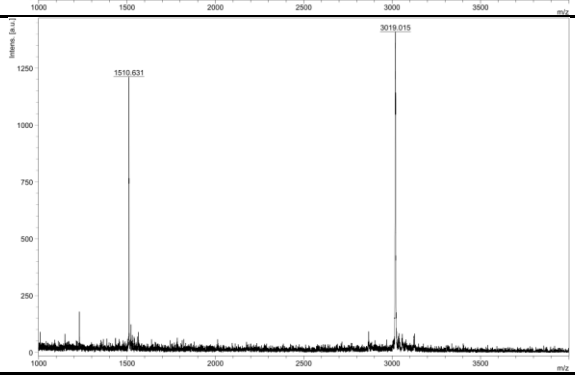
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.7
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.1

CPG-oligonucleotide + SeO_2

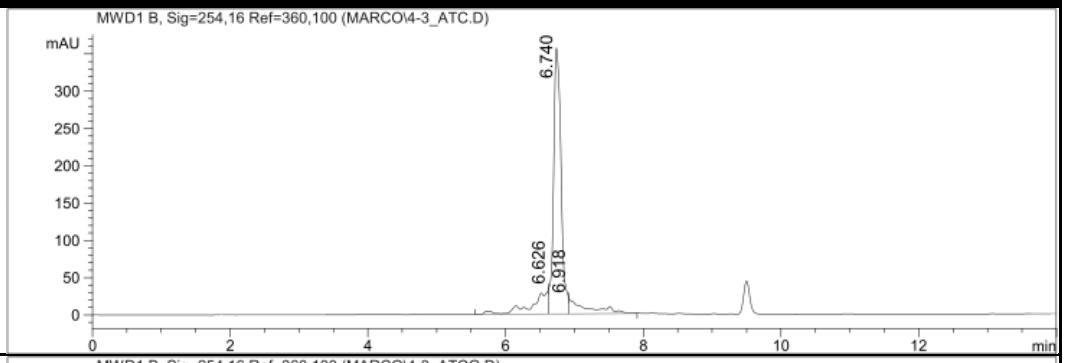
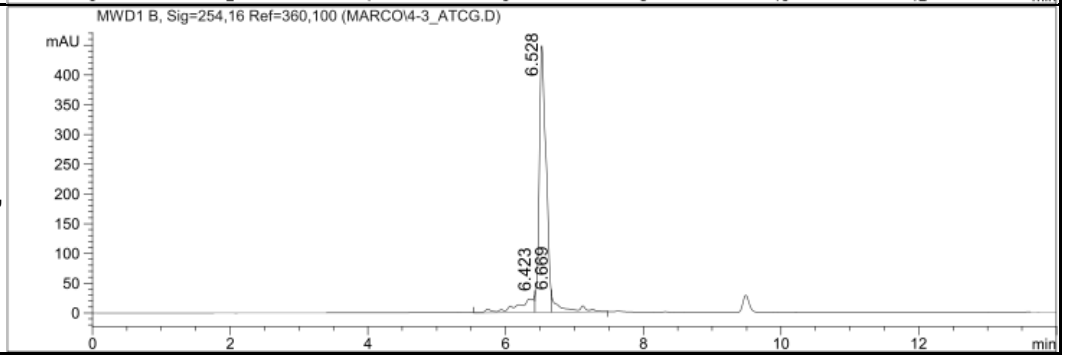
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with SeO_2 (200 equiv., 4 µmol) in dry MeOH at 40 °C.

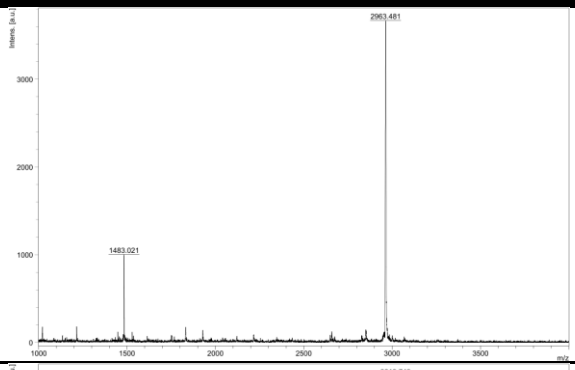
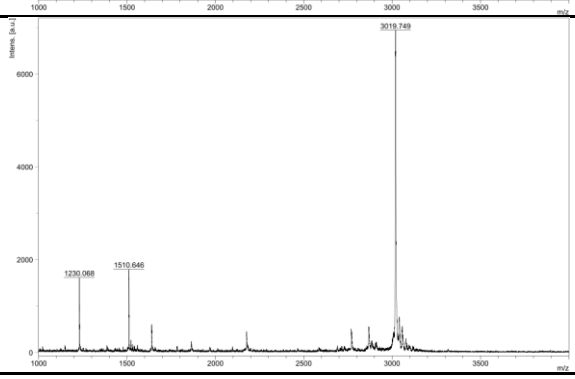
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.0

CPG-oligonucleotide + $Yb(OTf)_3$

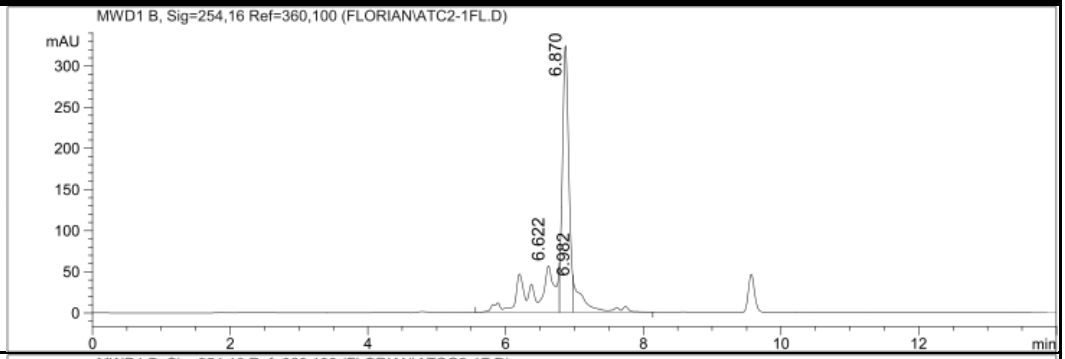
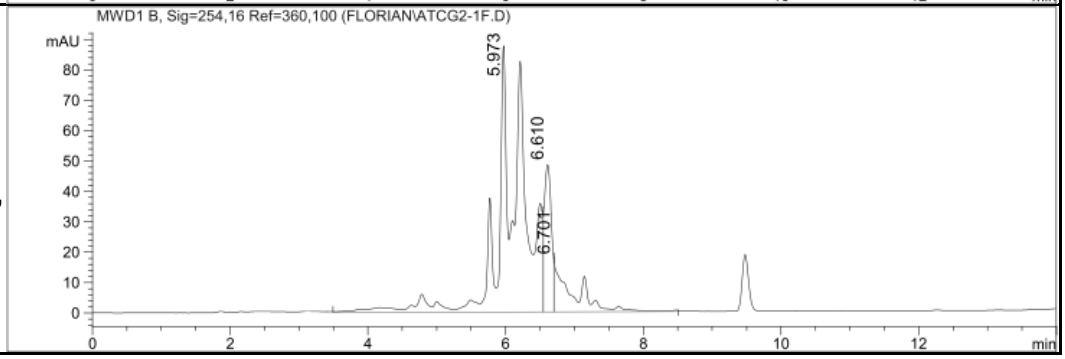
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Yb(OTf)_3$ (200 equiv., 4 µmol) in dry MeOH at 40 °C.

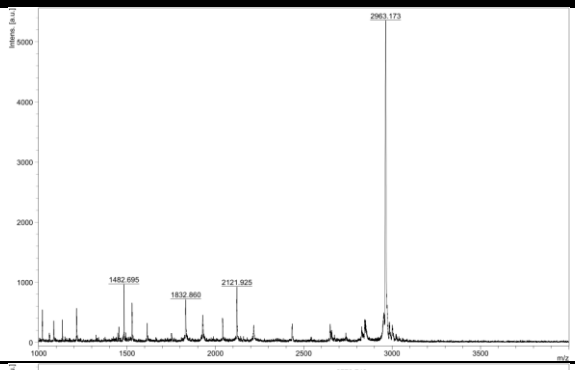
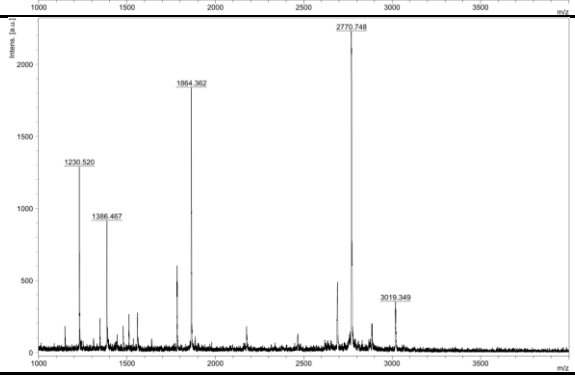
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.5
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.7

CPG-oligonucleotide + $Sc(OTf)_3$

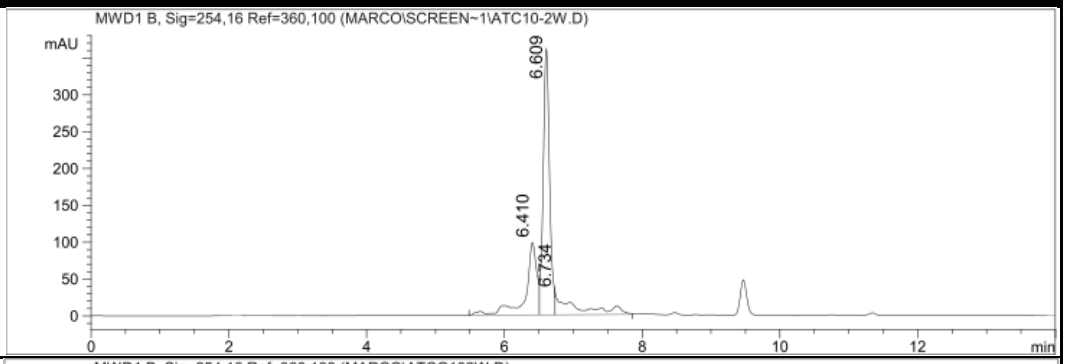
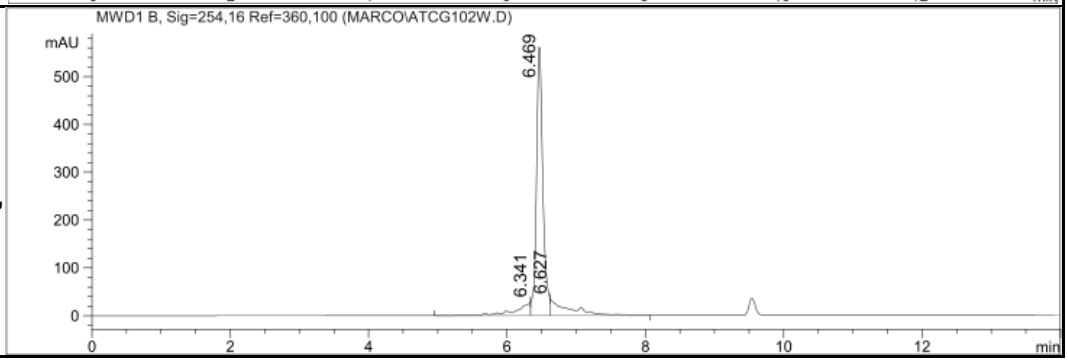
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Sc(OTf)_3$ (200 equiv., 4 µmol) in dry ACN at 40 °C.

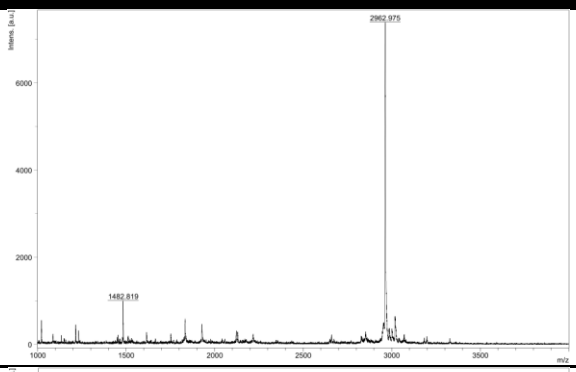
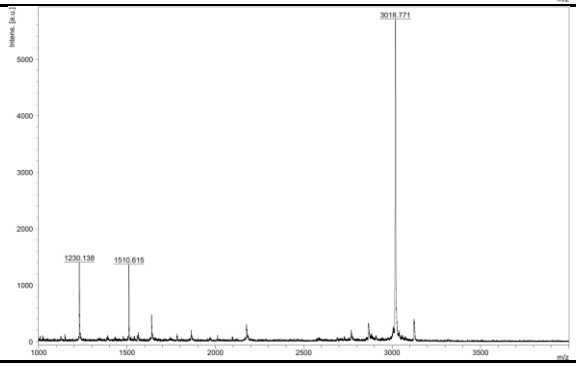
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.2
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.3

CPG-oligonucleotide + AgOTf

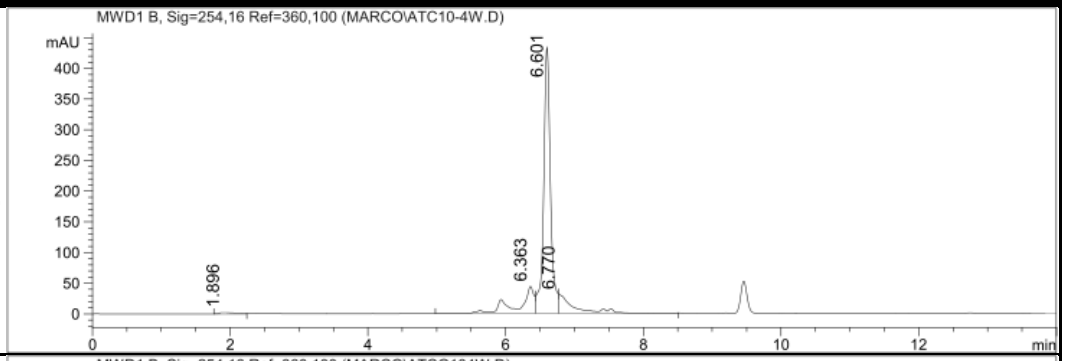
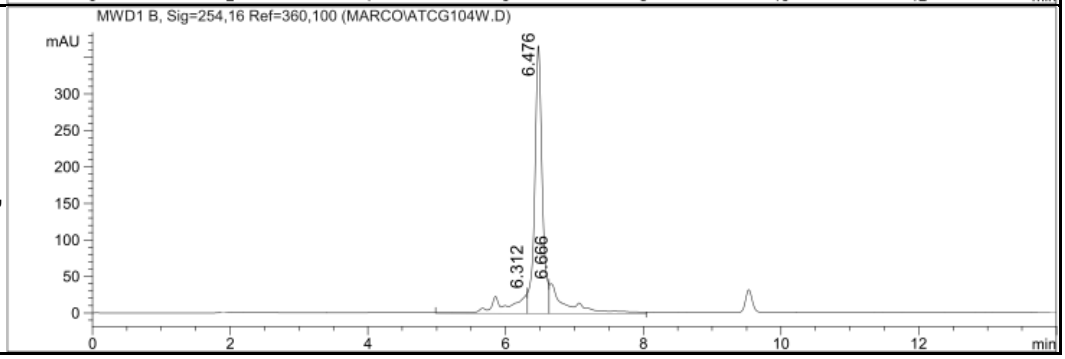
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with AgOTf (200 equiv., 4 µmol) in HPLC-grade ACN.

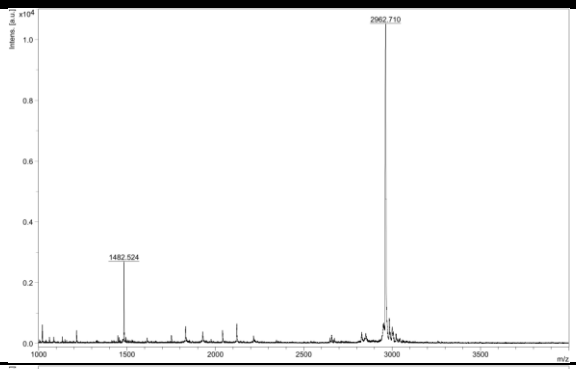
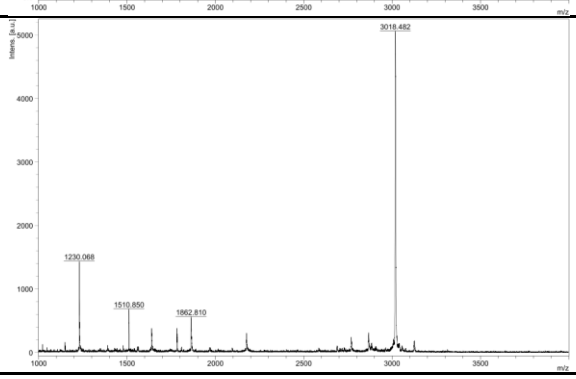
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.8

CPG-oligonucleotide + $BiBr_3$

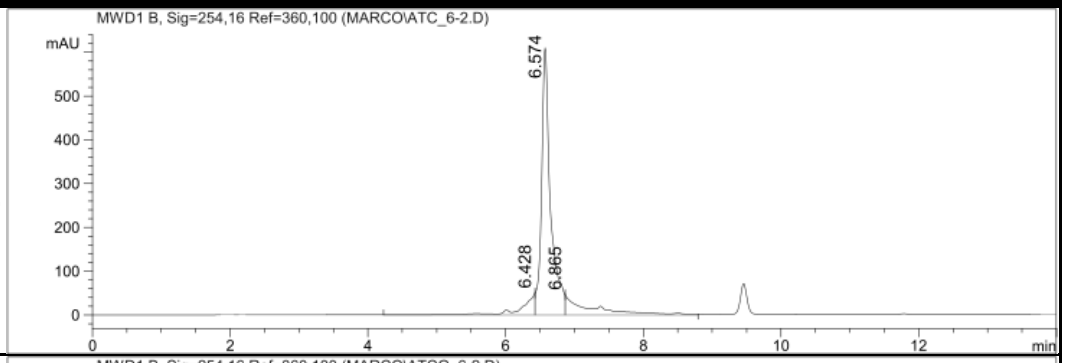
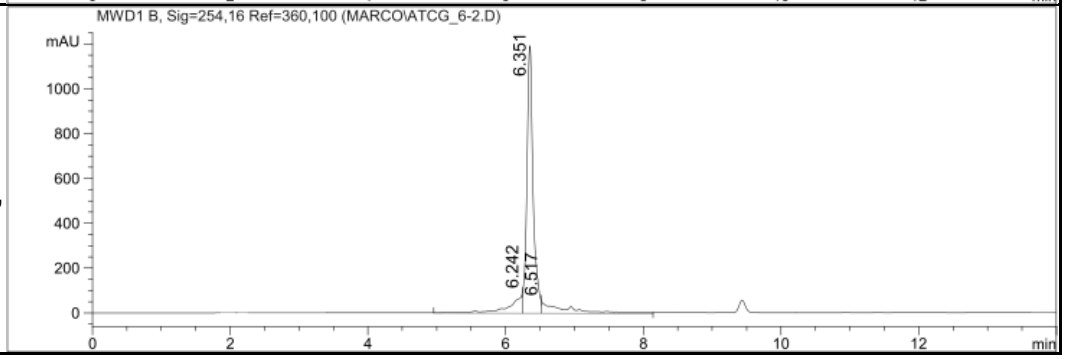
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $BiBr_3$ (200 equiv., 4 µmol) in HPLC-grade ACN.

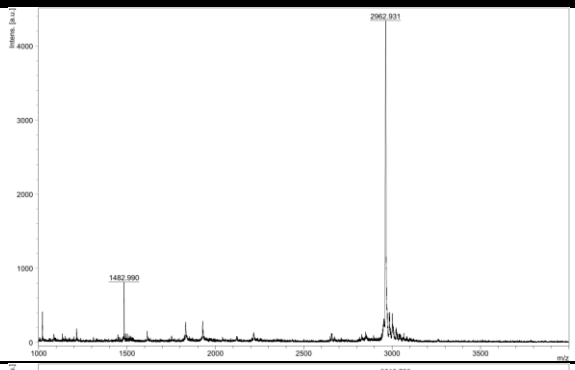
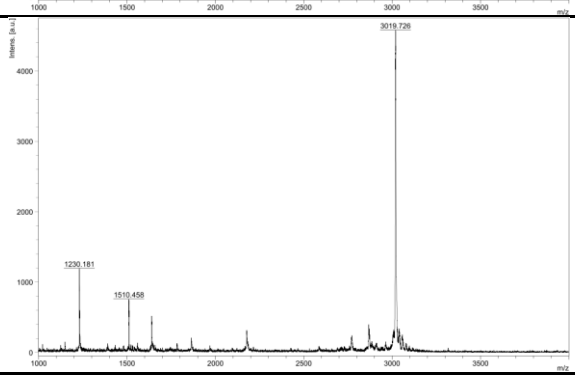
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.7
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.5

CPG-oligonucleotide + $InCl_3$

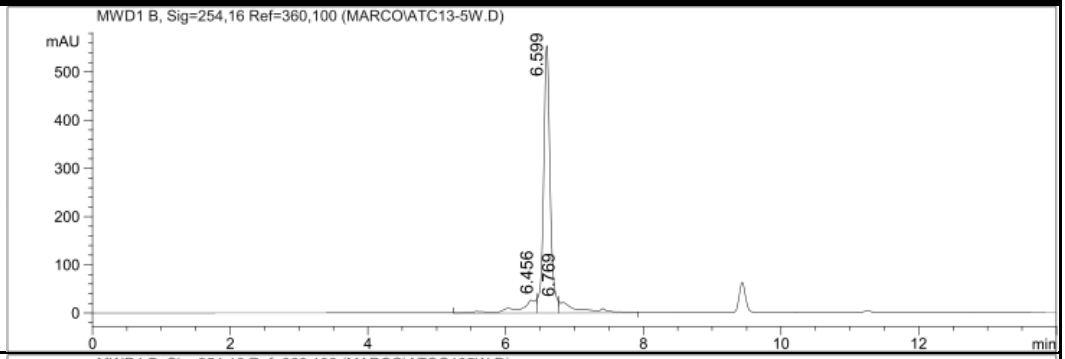
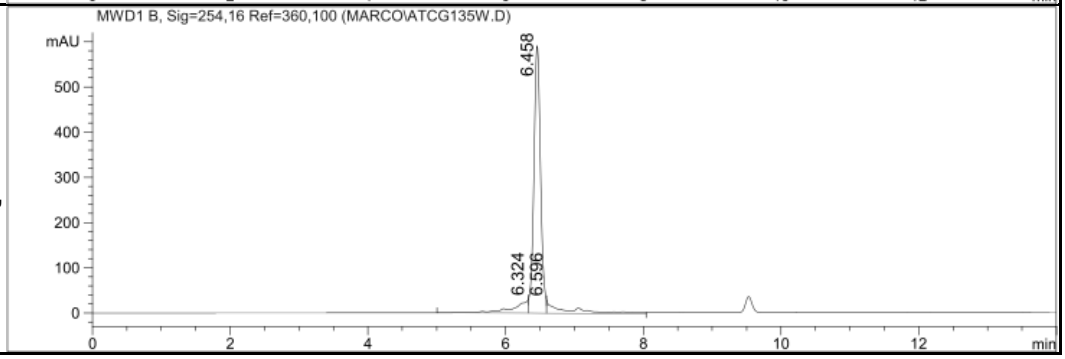
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $InCl_3$ (200 equiv., 4 µmol) in HPLC-grade ACN.

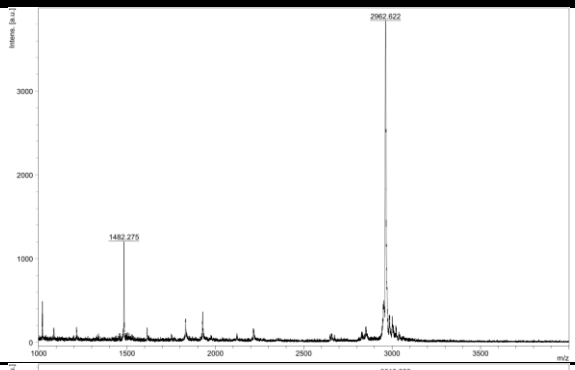
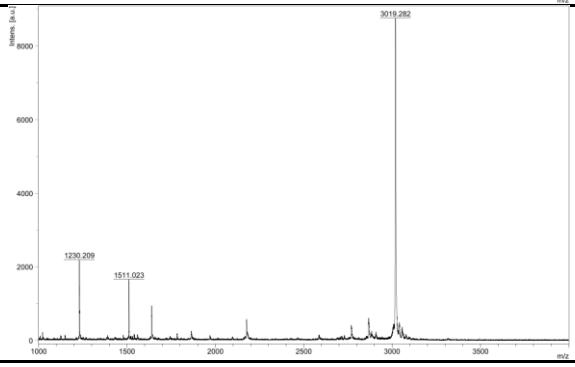
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.9
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.7

CPG-oligonucleotide + LiBr

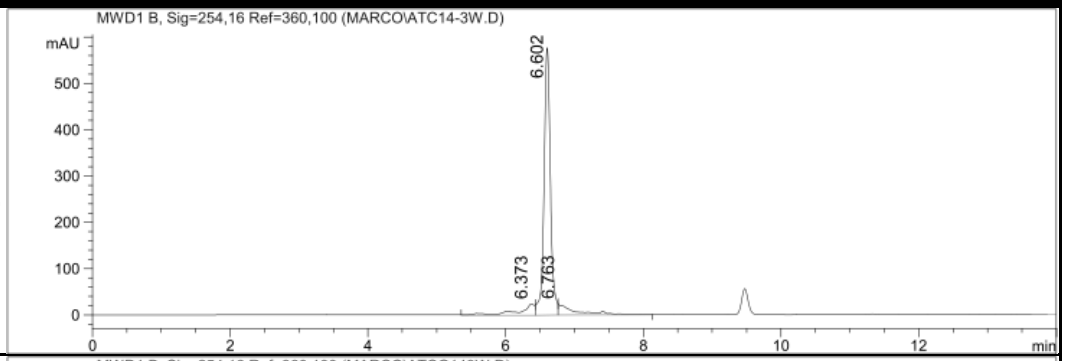
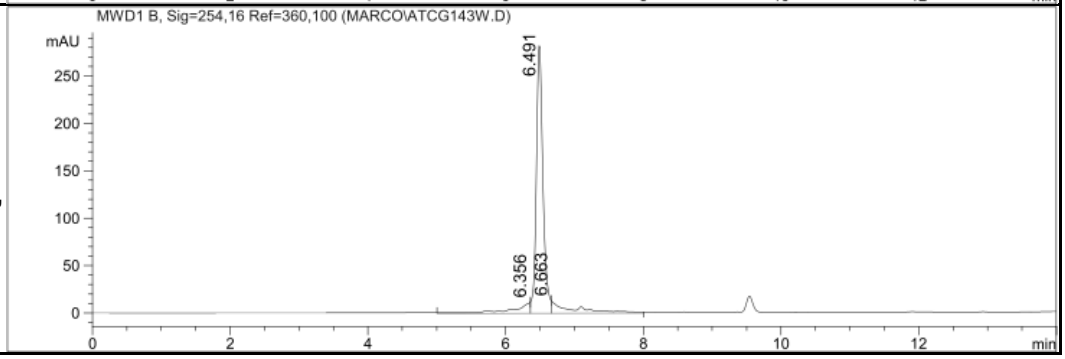
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with LiBr (200 equiv., 4 µmol) in HPLC-grade ACN.

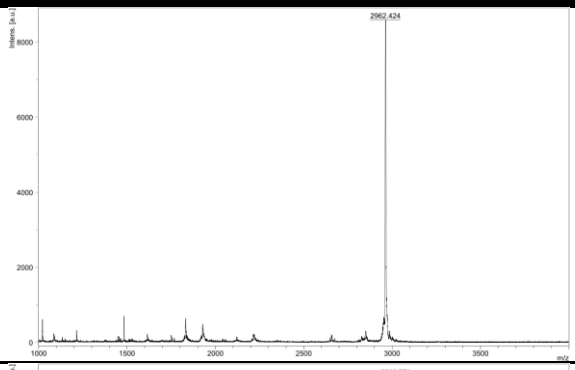
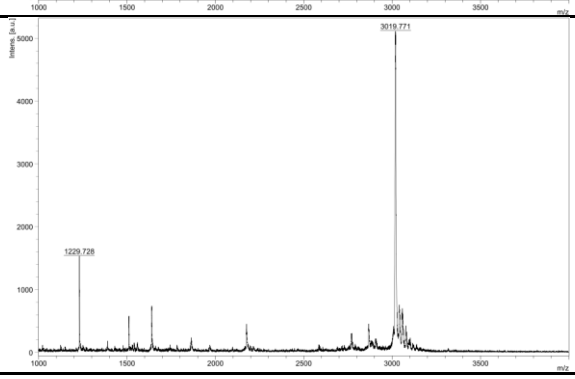
CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.6
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.3

CPG-oligonucleotide + Ni(acac)$_2$

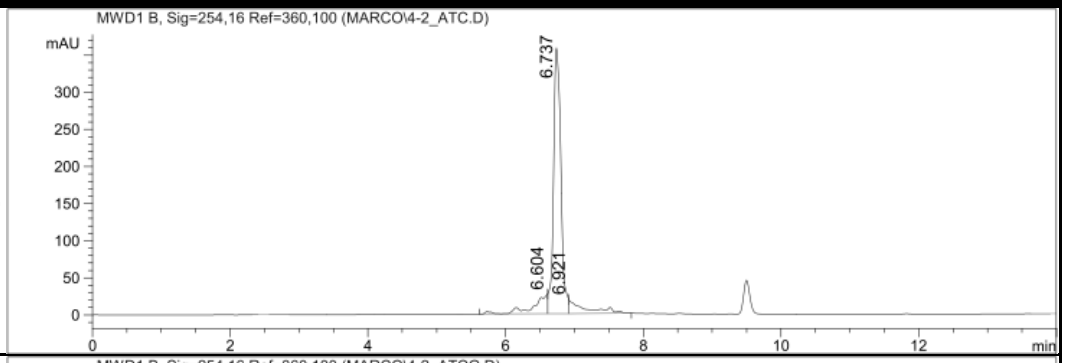
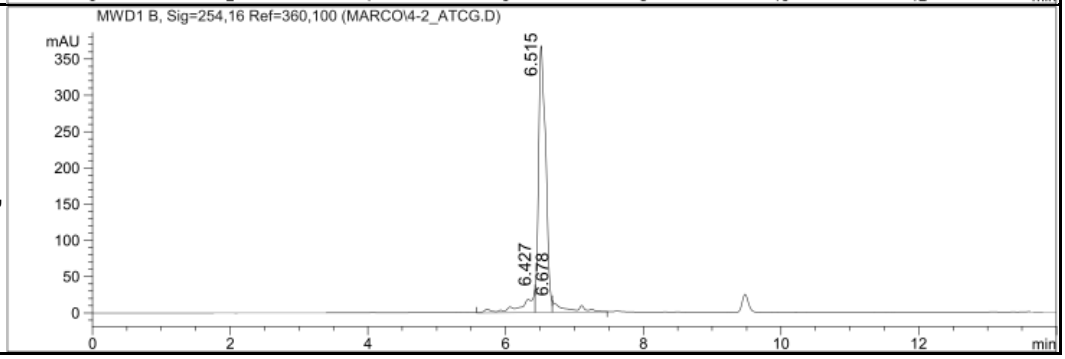
According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with Ni(acac)$_2$ (200 equiv., 4 µmol) in HPLC-grade ACN.

CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.4
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.8

CPG-oligonucleotide + $Yb(OTf)_3$

According to the representative procedure (RP-03) solid support coupled oligonucleotide (20 nmol) was treated with $Yb(OTf)_3$ (200 equiv., 4 µmol) in HPLC-grade MeOH.

CPG-oligonucleotide	Analytical RP-HPLC-trace
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

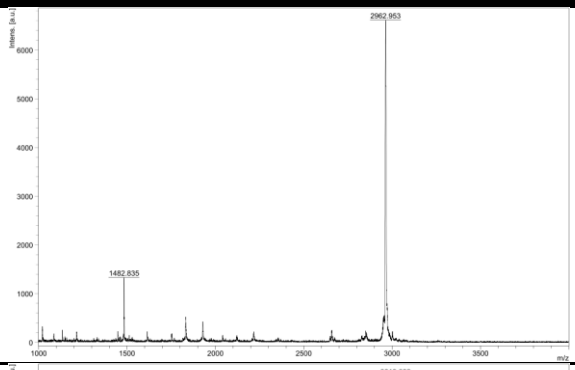
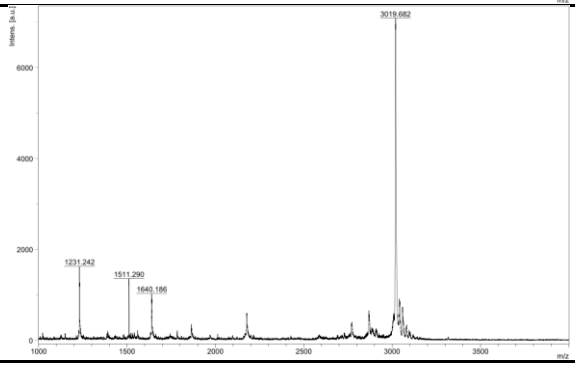
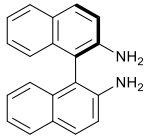
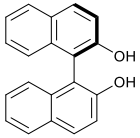
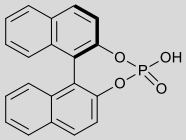
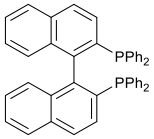
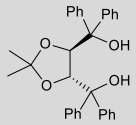
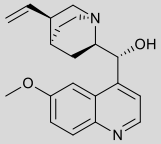
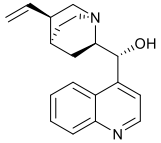
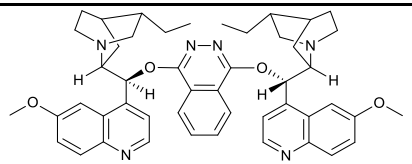
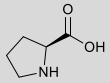
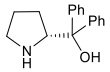
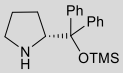
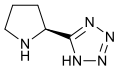
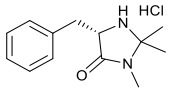
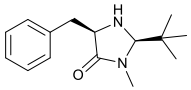
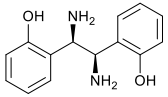
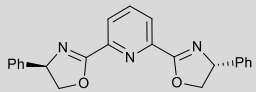
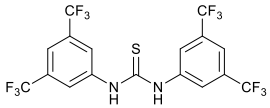
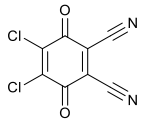
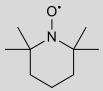
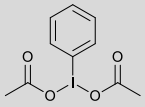
CPG-oligonucleotide	MALDI-MS spectra	
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.7

Table S4 – Stability of DNA against organocatalysts and organic reagents[a]

Entry[a]	Organo Catalyst	No.	Solvent	hexT	TC	ATC	ATCG
1		**I**	MeOH				
2		**J**	ACN				
3		**A**	MeOH				
4		**K**	MeOH				
5		**B**	MeOH				
6		**C**	MeOH				
7		**L**	MeOH				

8		**M**	MeOH				
9		**D**	ACN				
10		**N**	ACN				
11		**E**	MeOH				
12		**O**	MeOH				
13		**P**	MeOH				
14		**Q**	ACN				
15		**R**	MeOH				

16		**F**	ACN				
17		**S**	MeOH				
18		**T**	EtOH				
19		**G**	ACN				
20		**H**	ACN				

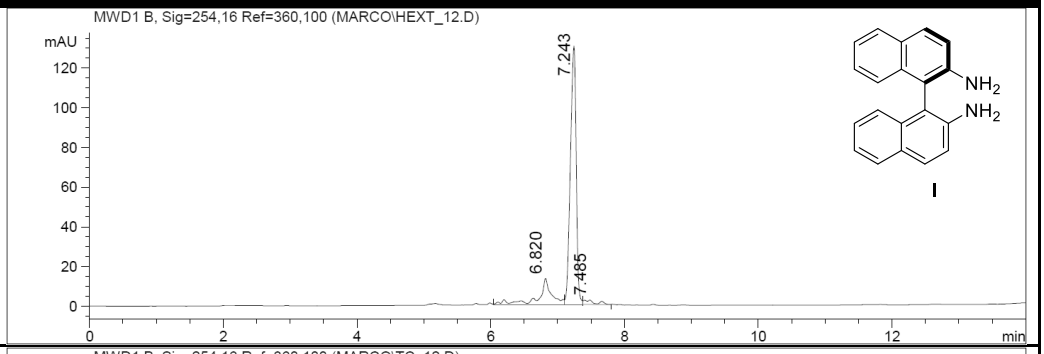
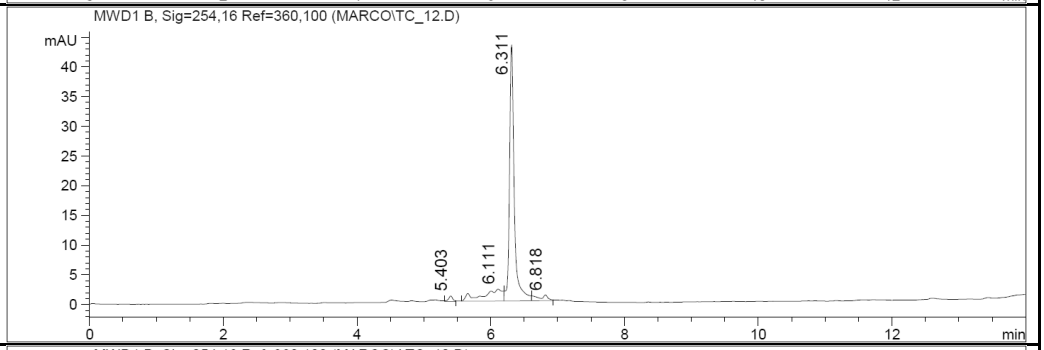
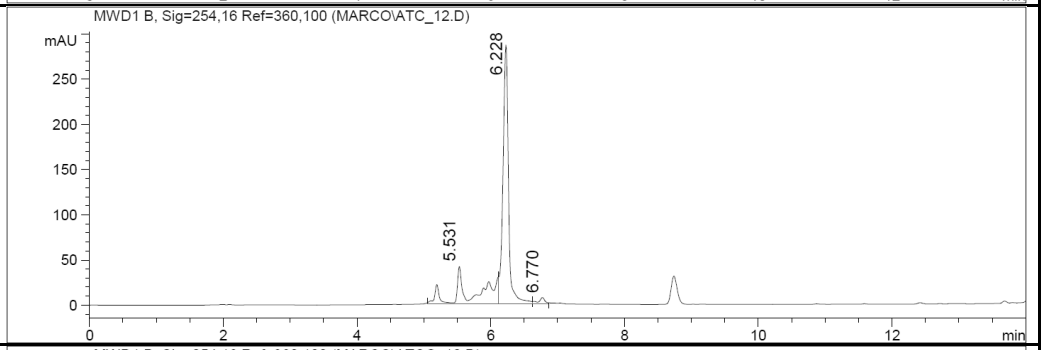
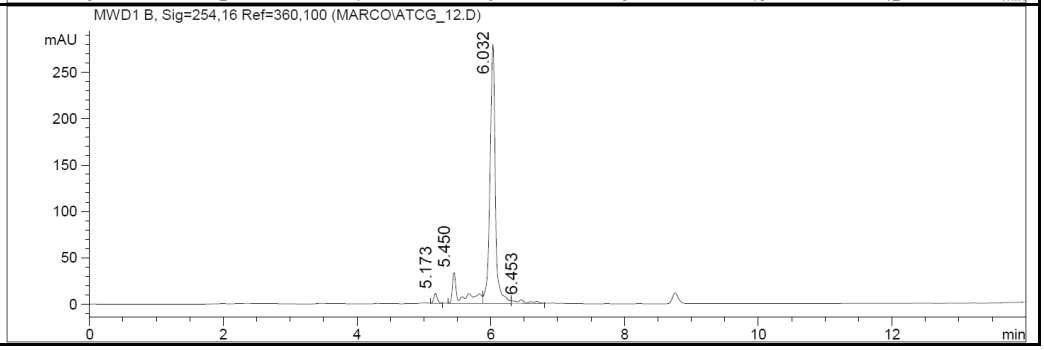
[a] for each: 20 nmol DNA, 200 eq. organo catalyst, 50 µL solvent, r.t., 22 h; EtOH = ethanol, ACN = acetonitrile, MeOH = methanol.

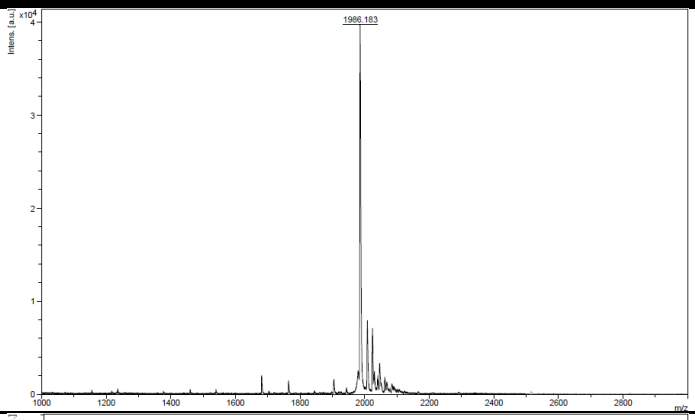
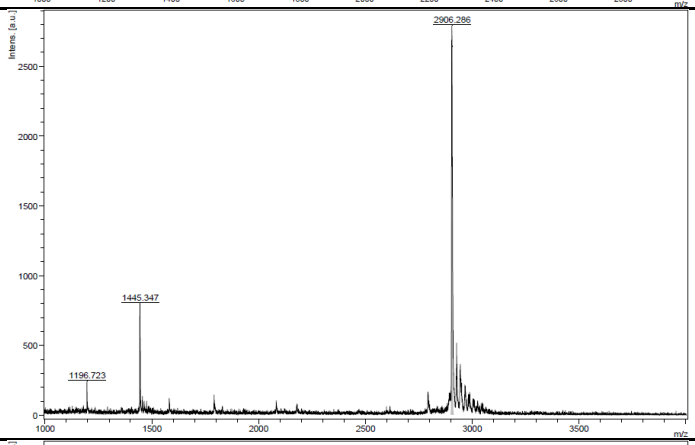
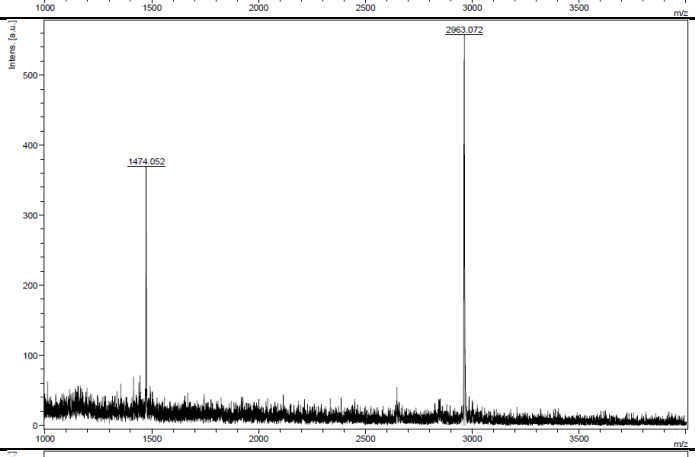
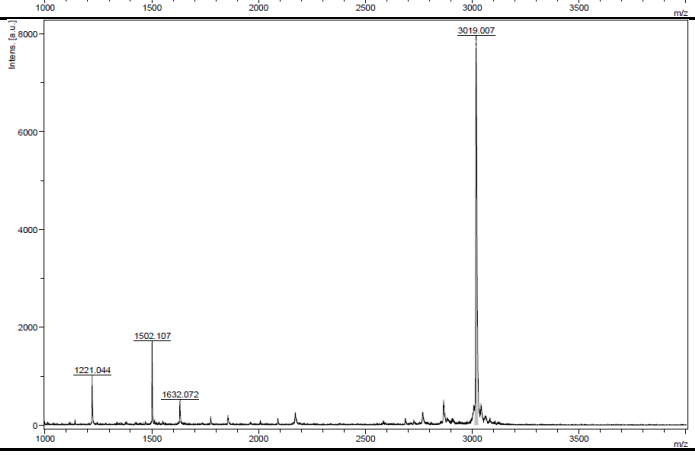
				DNA degradation
0-20%	21-40%	41-60%	> 61%	

HPLC traces and MALDI-MS spectra of organocatalyst and organic reagents screens

CPG-oligonucleotide + (*R*)-(+)-DABN I

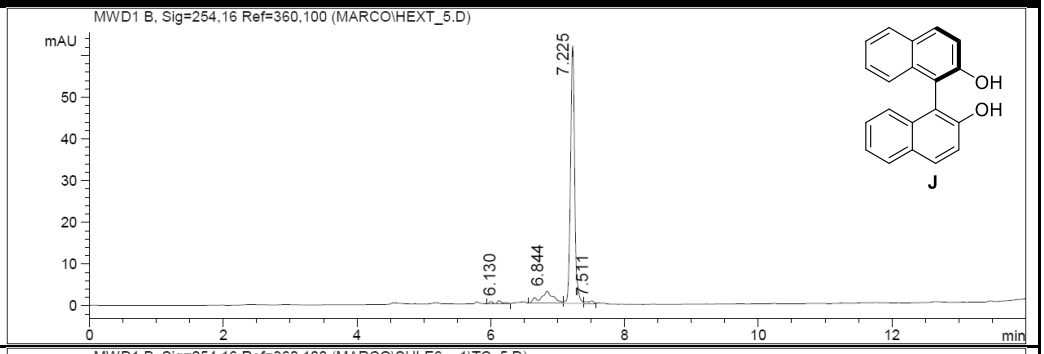
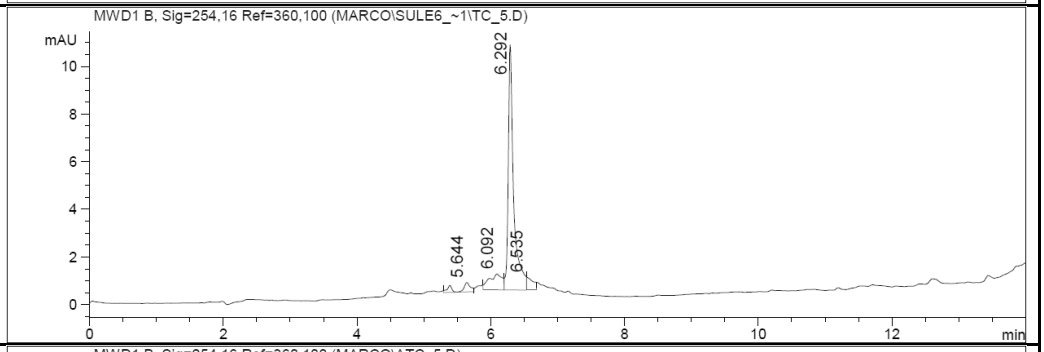
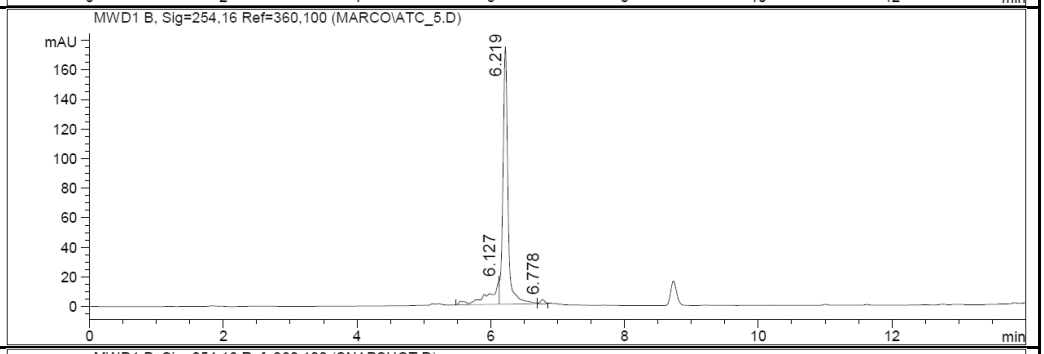
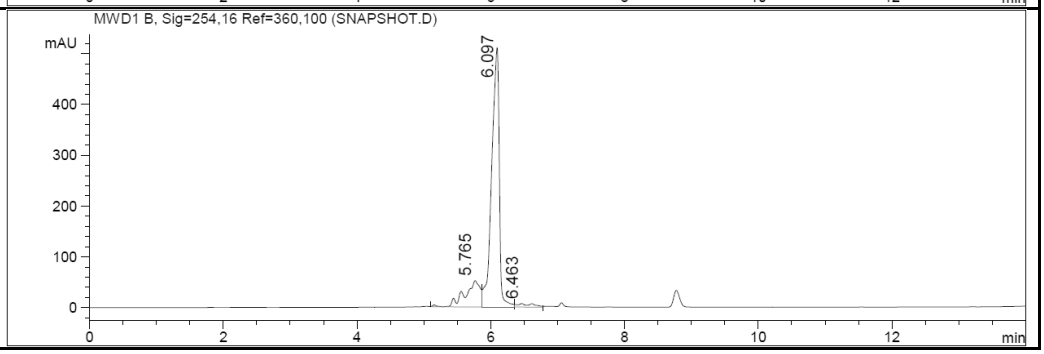
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (*R*)-(+)-DABN **I** (200 equiv., 4 µmol) in dry MeOH.

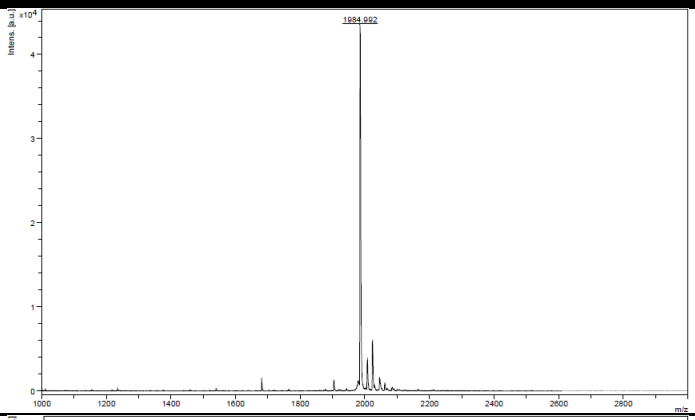
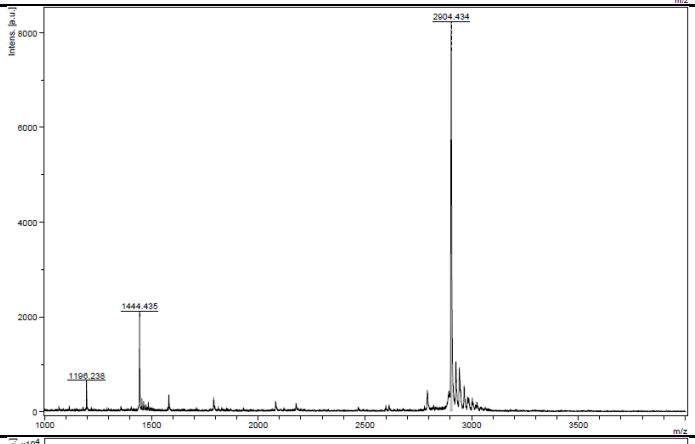
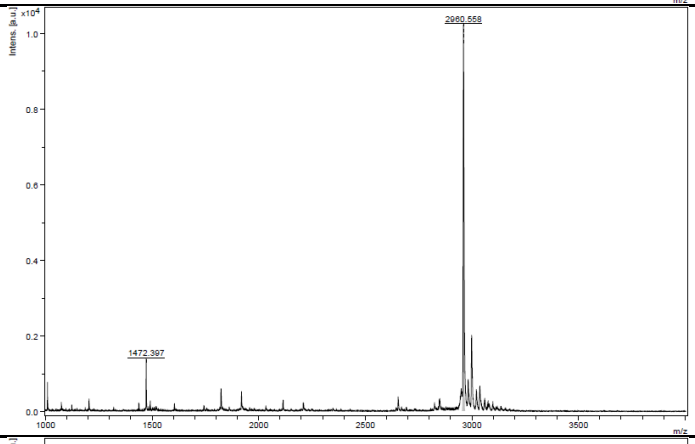
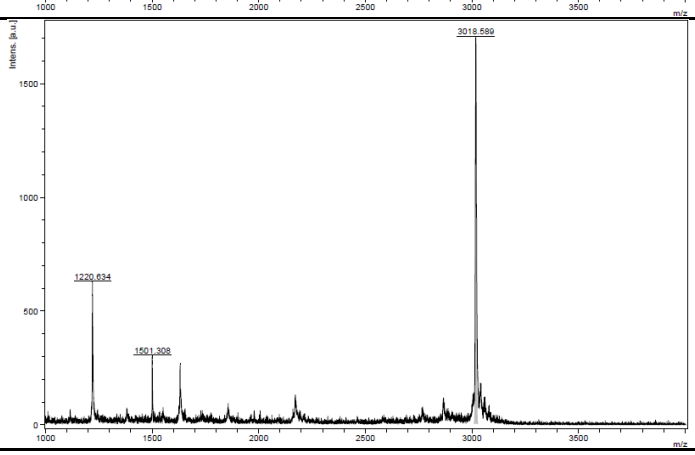
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2906.3
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.1
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.0

CPG-oligonucleotide + (*R*)-BINOL J

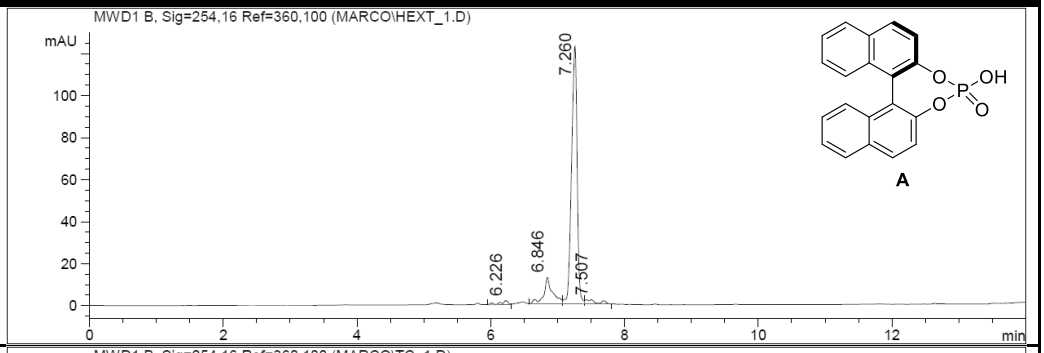
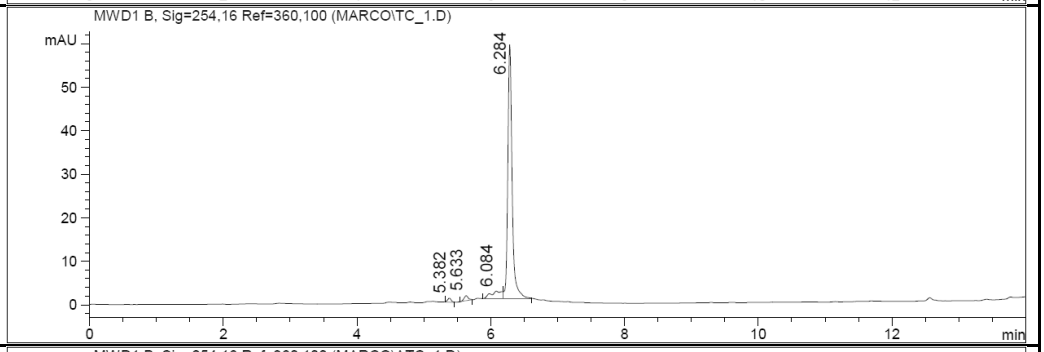
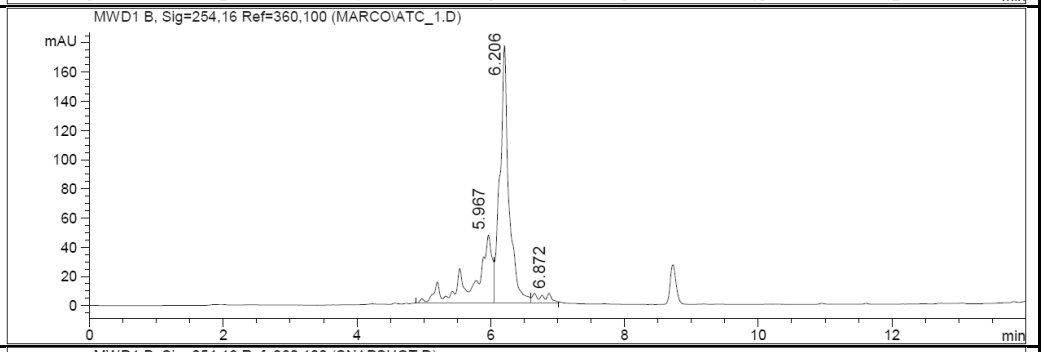
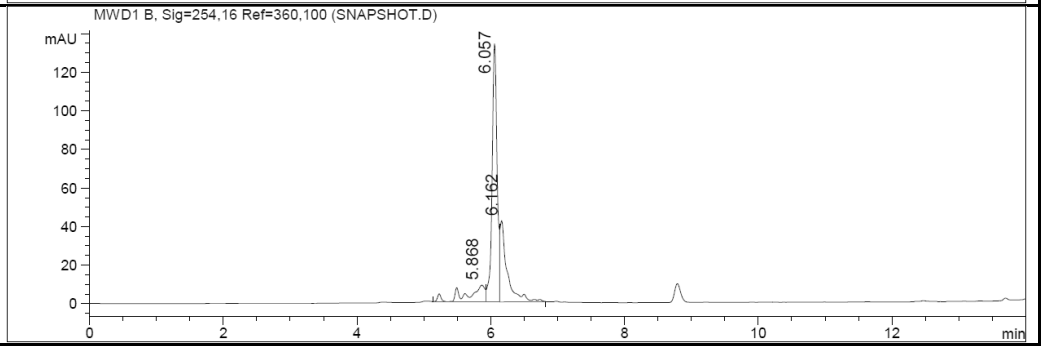
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with ((*R*)-BINOL **J** (200 equiv., 4 µmol) in dry ACN.

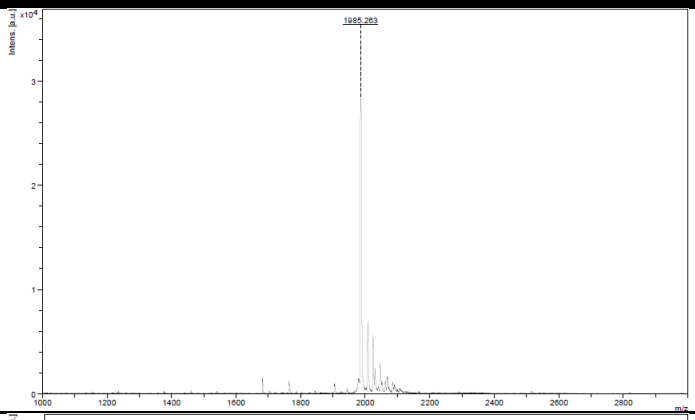
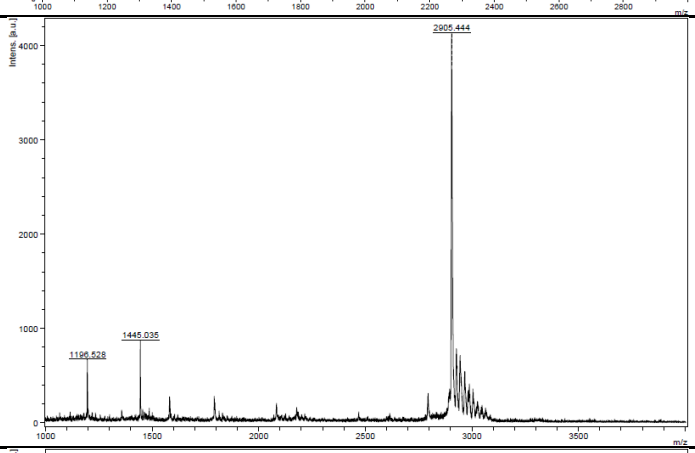
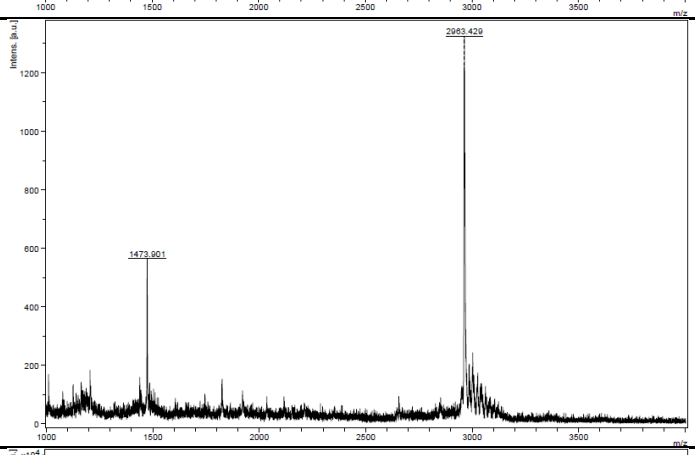
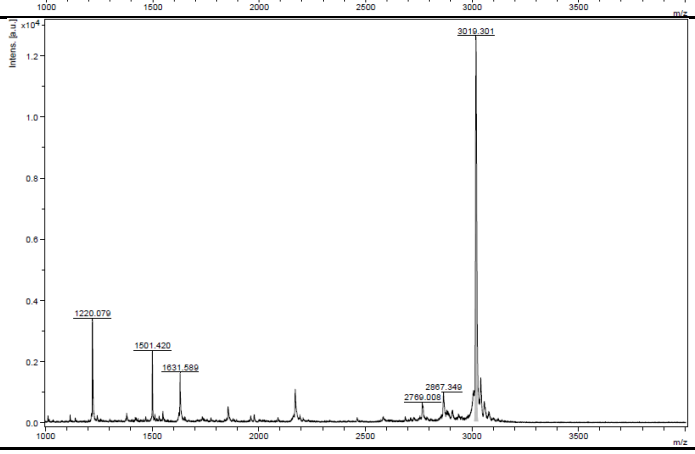
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2960.6
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

CPG-oligonucleotide + (*R*)-1,1-Binaphthyl-2,2-diyl hydrogenphosphate A

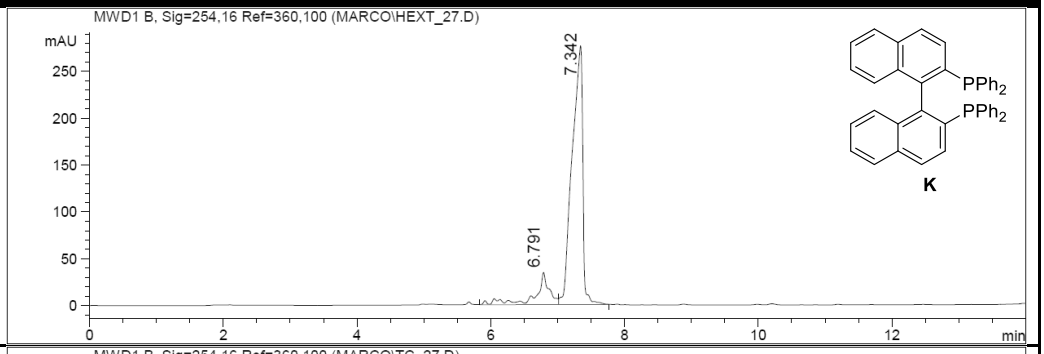
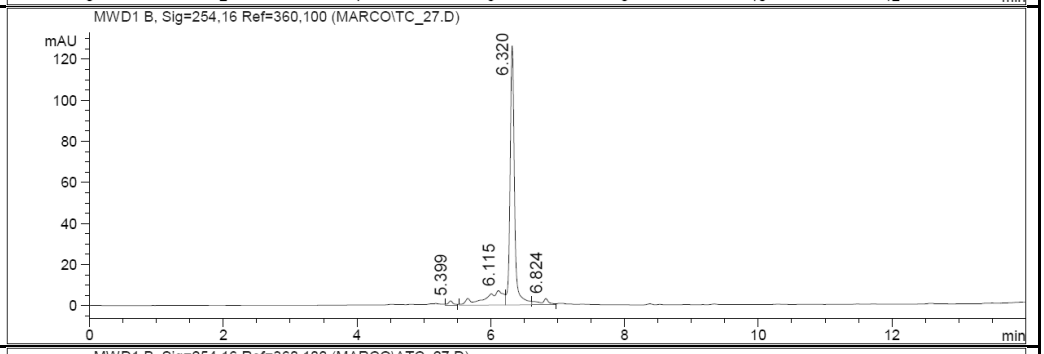
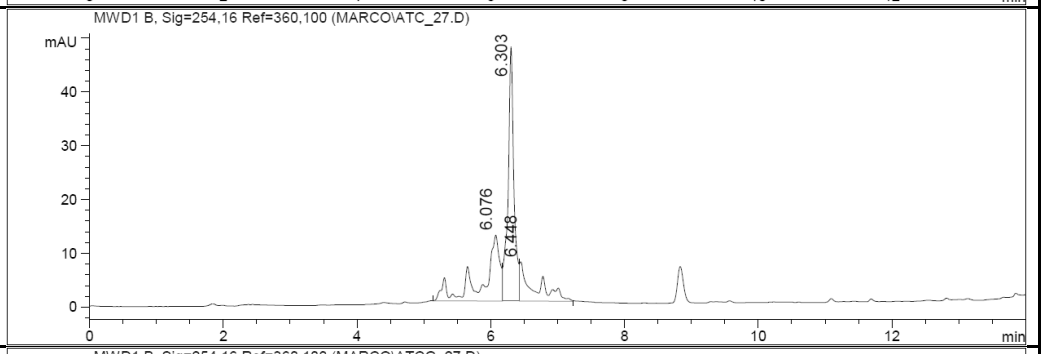
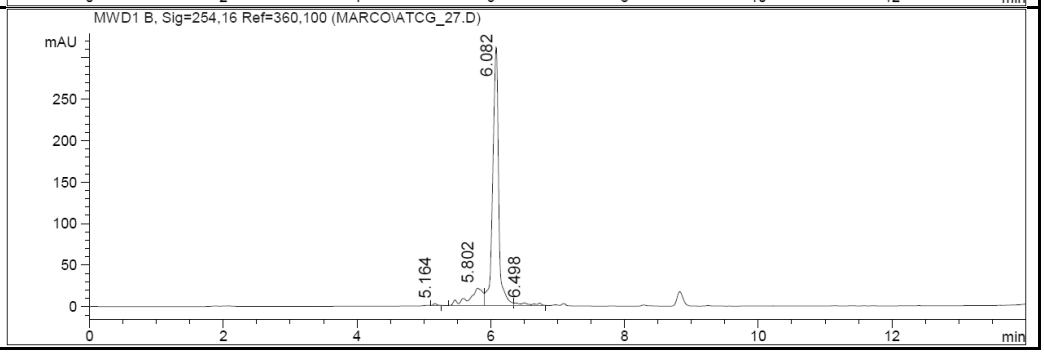
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (*R*)-1,1-Binaphthyl-2,2-diyl hydrogenphosphate **A** (200 equiv., 4 µmol) in dry MeOH.

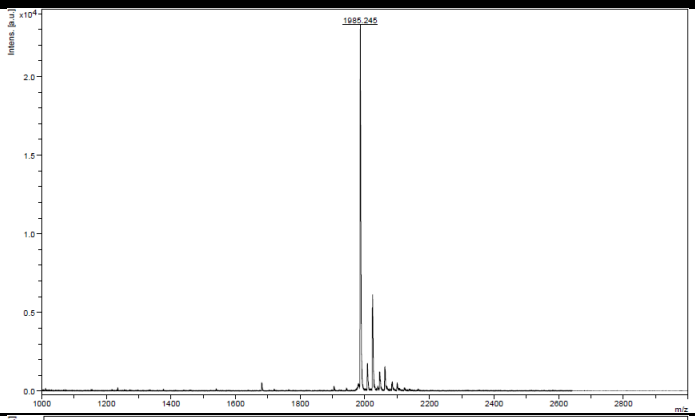
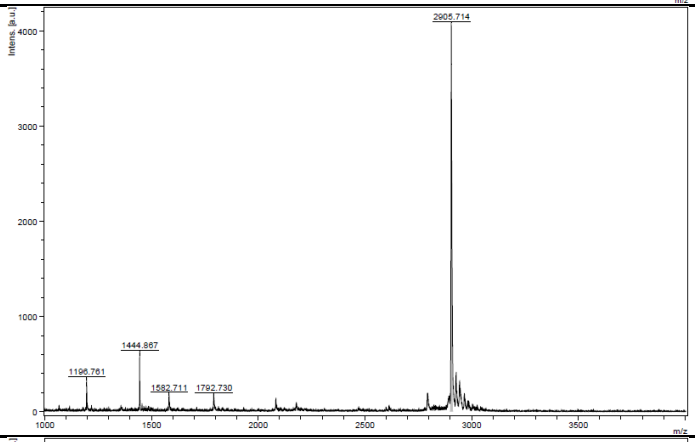
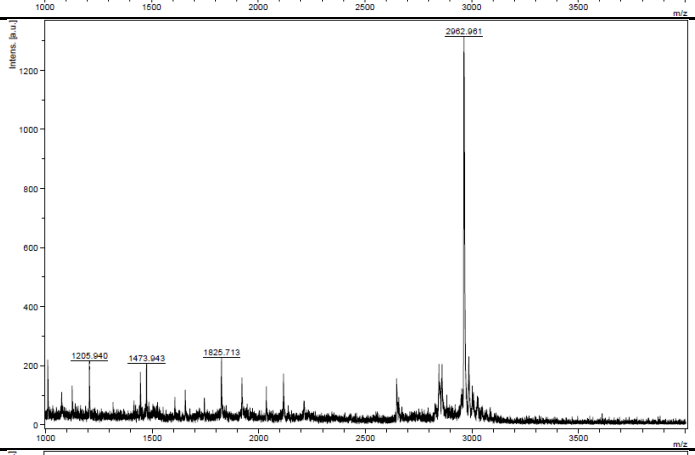
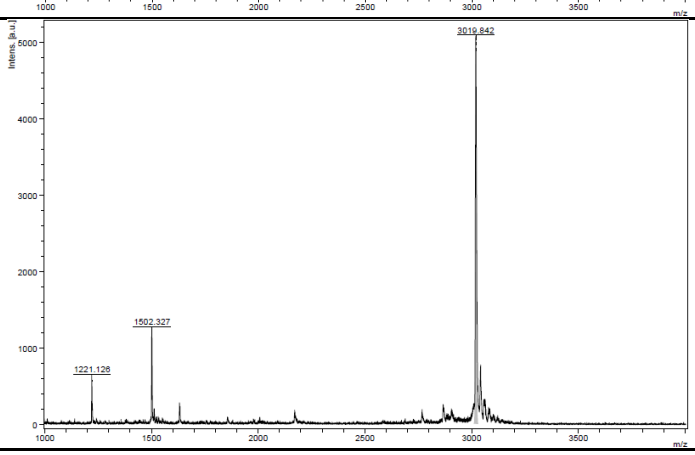
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.4
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.3

CPG-oligonucleotide + (±)-BINAP K

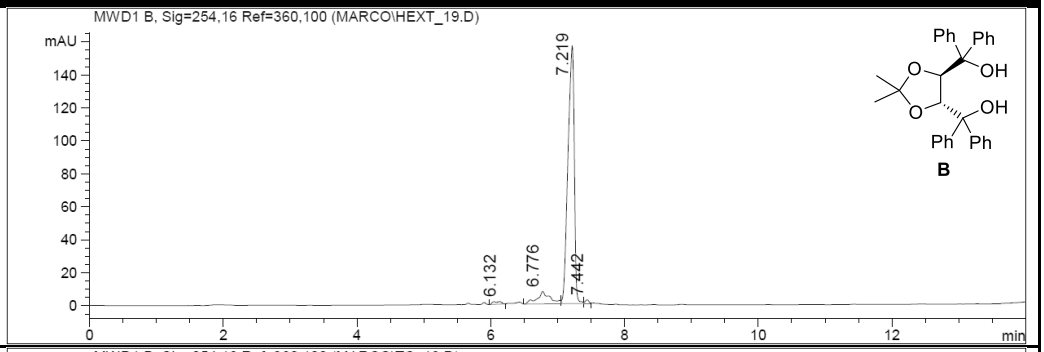
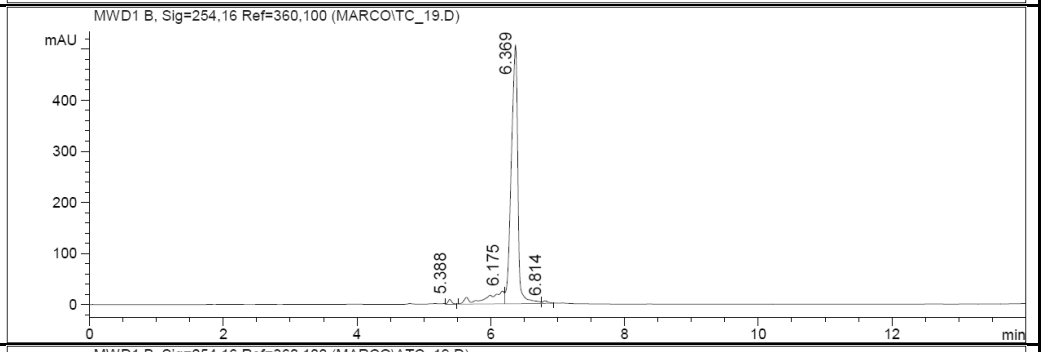
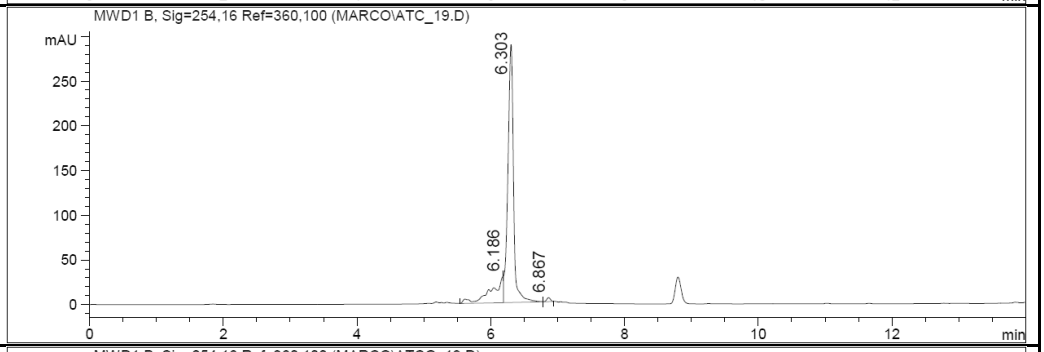
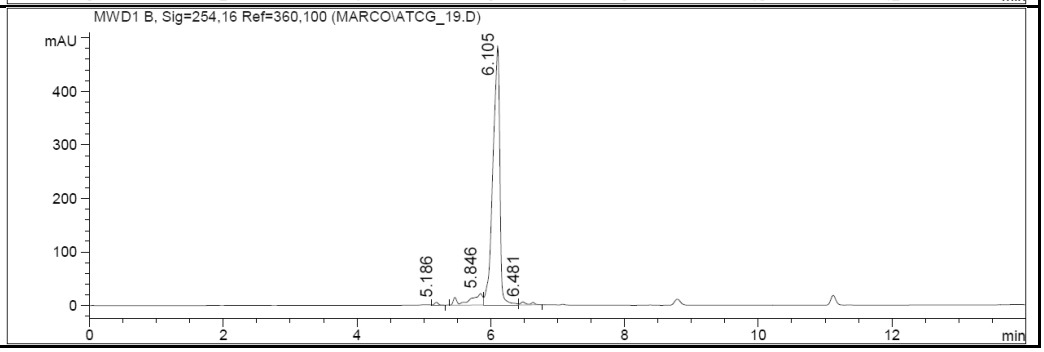
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (±)-BINAP **K** (200 equiv., 4 µmol) in dry MeOH.

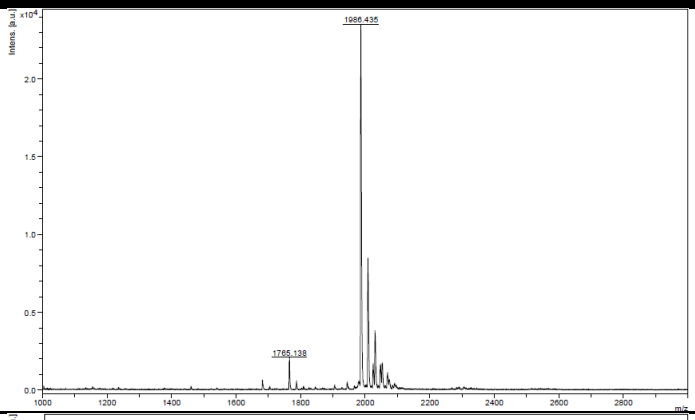
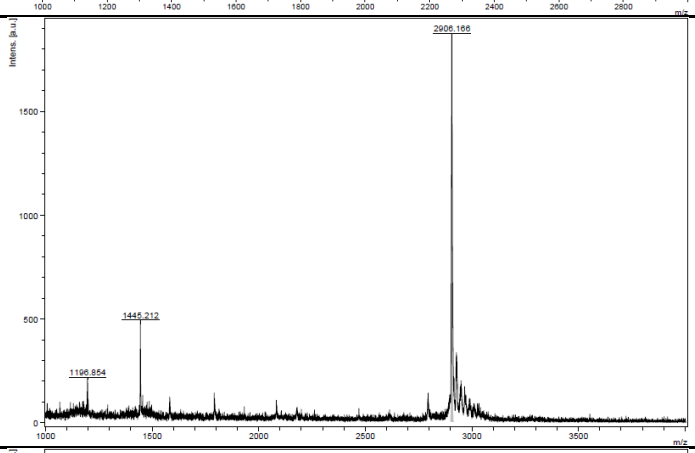
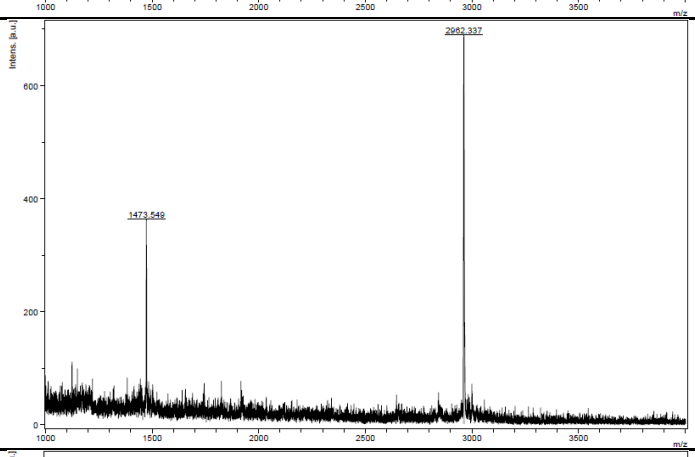
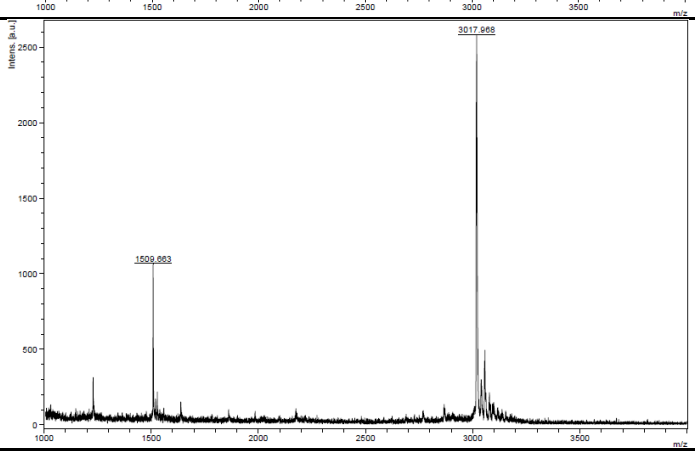
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.8

CPG-oligonucleotide + TADDOL B

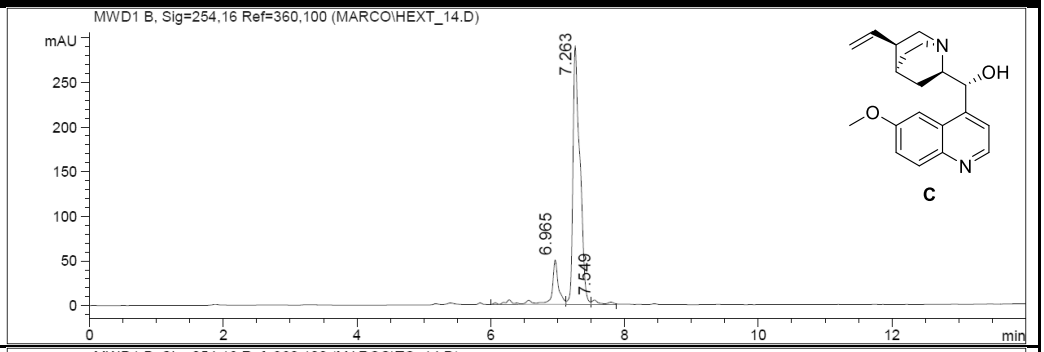
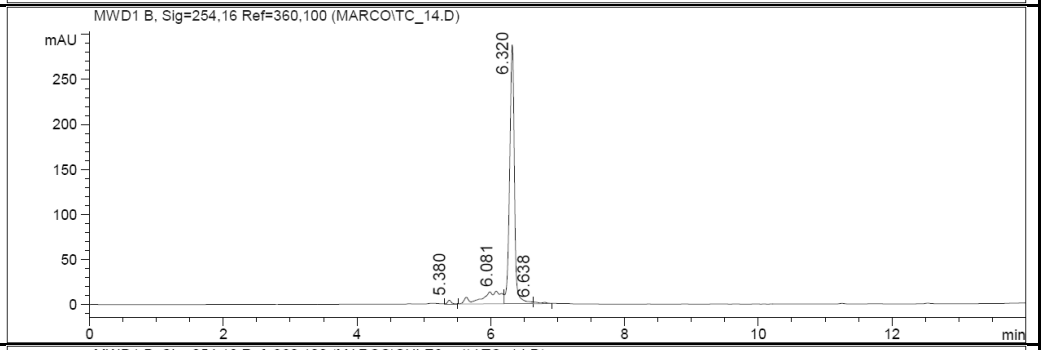
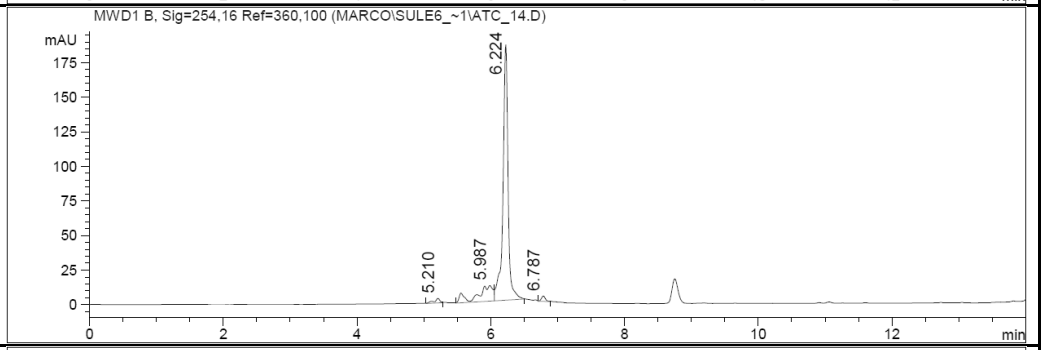
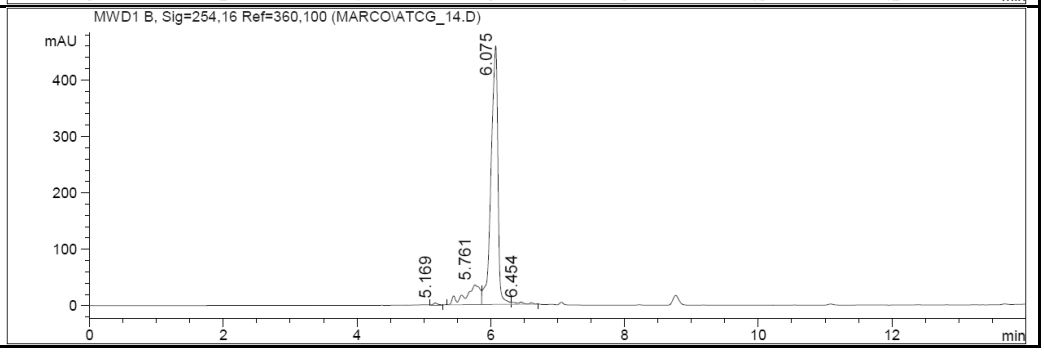
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with TADDOL **B** (200 equiv., 4 µmol) in dry MeOH.

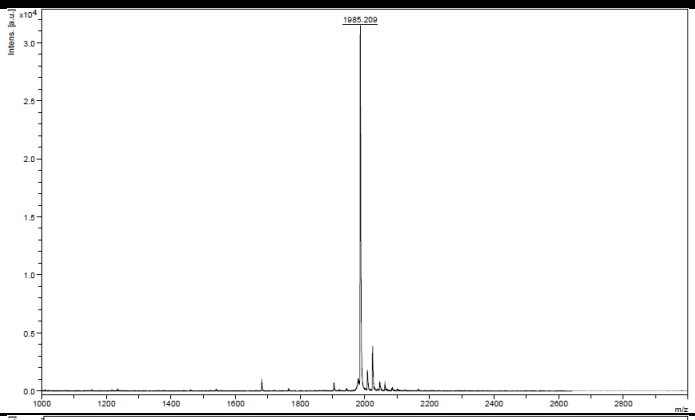
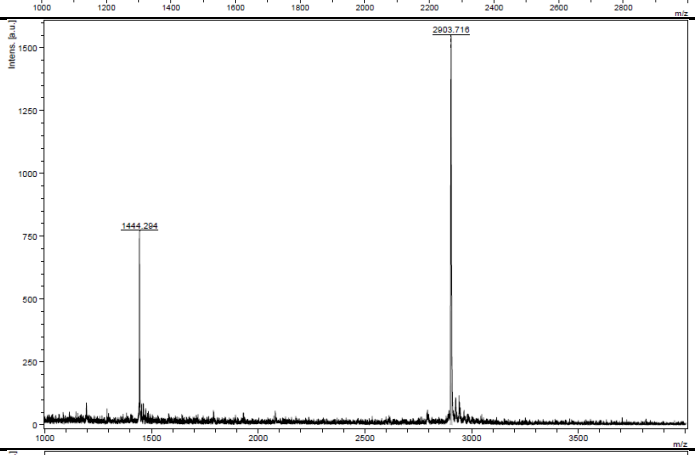
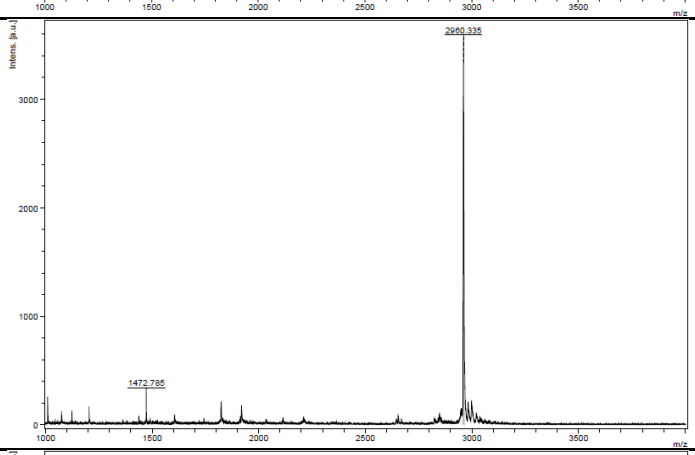
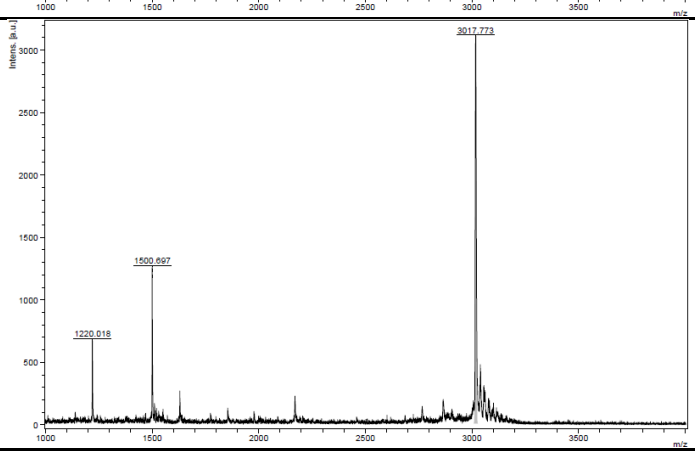
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.4
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2906.2
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.0

CPG-oligonucleotide + Quinine C

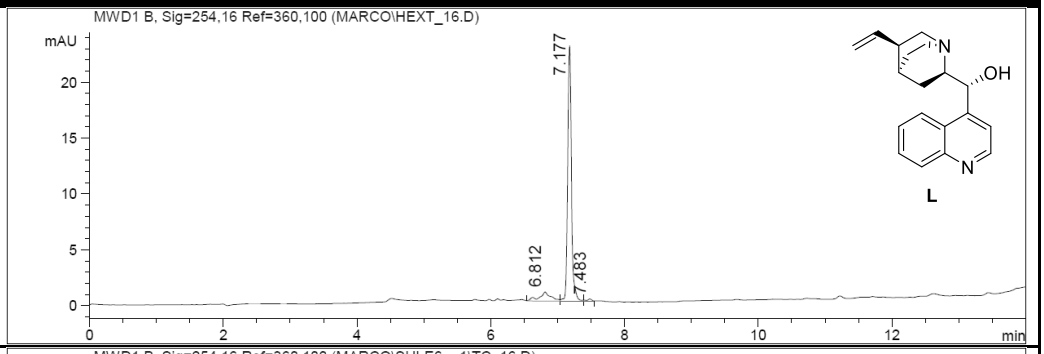
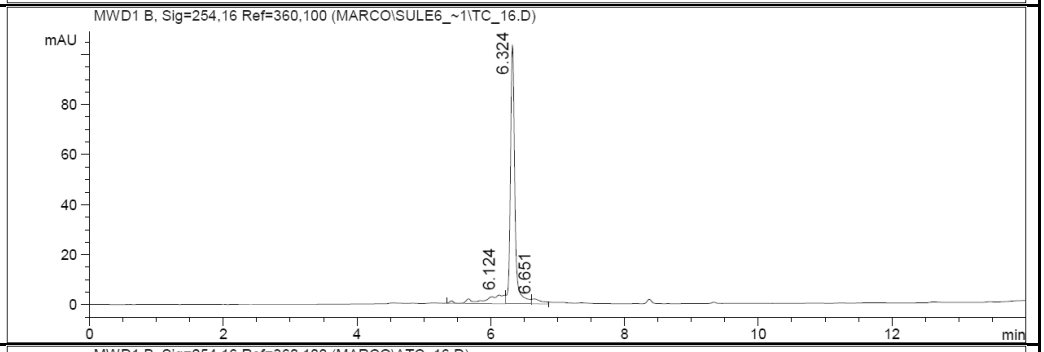
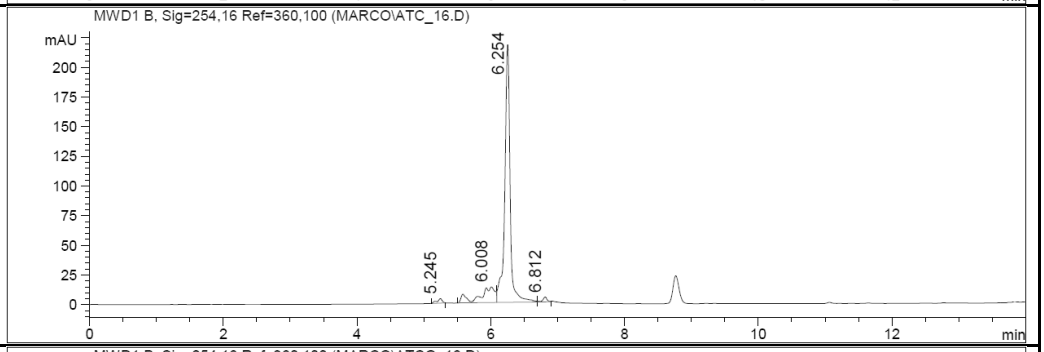
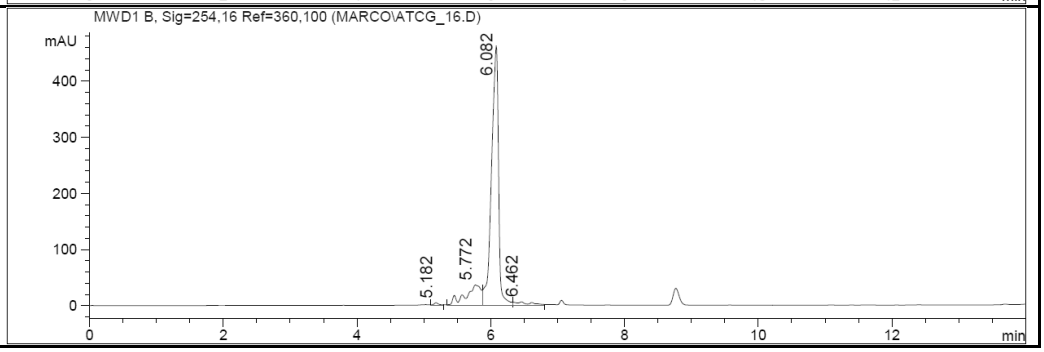
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with Quinine **C** (200 equiv., 4 µmol) in dry MeOH.

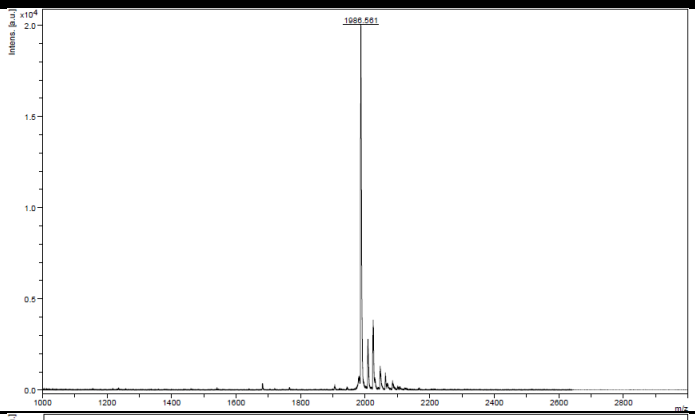
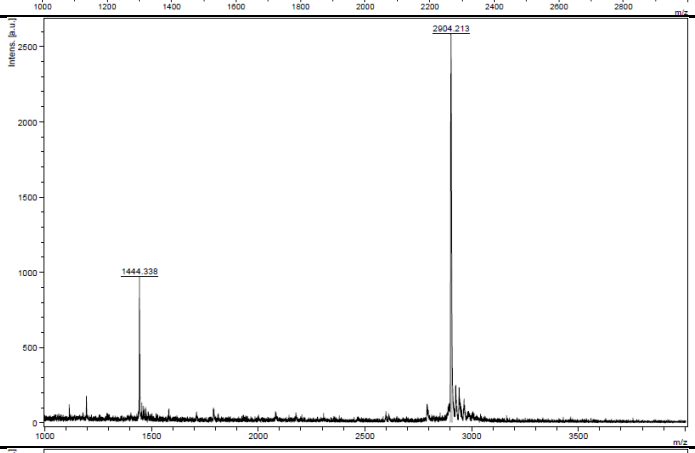
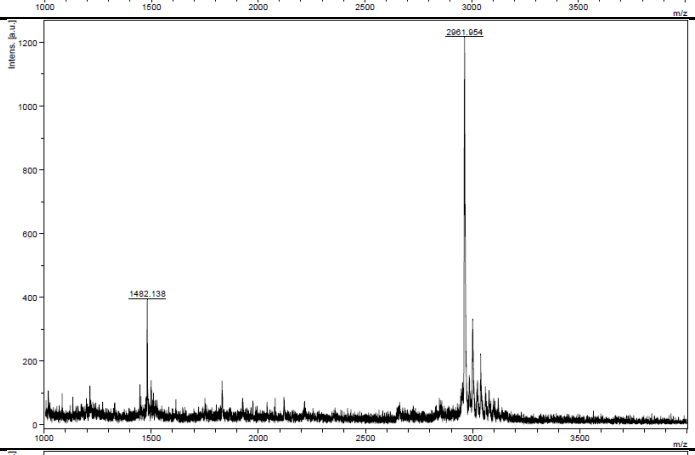
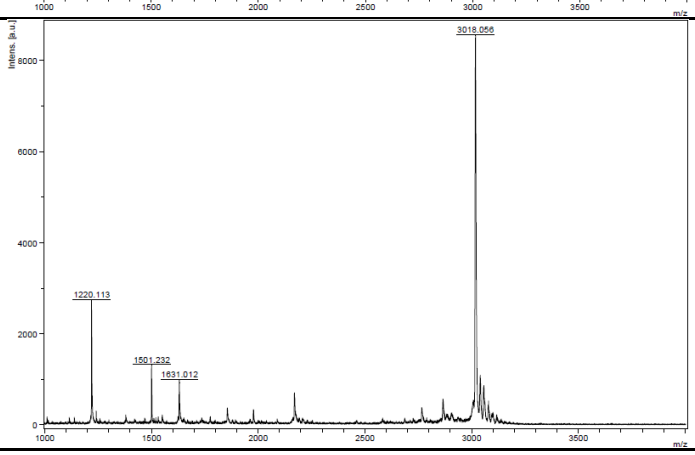
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2903.7
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2960.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.8

CPG-oligonucleotide + Cinchonidine L

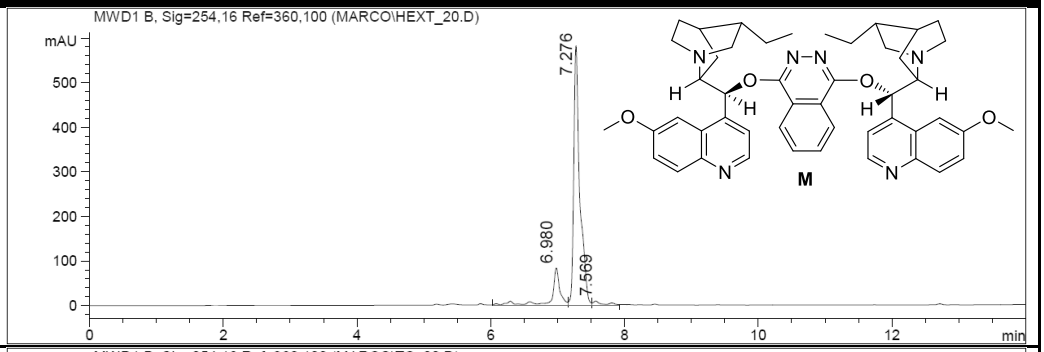
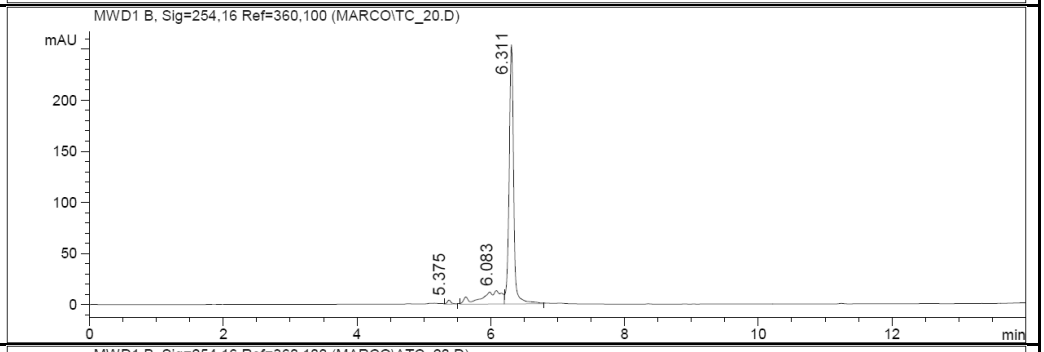
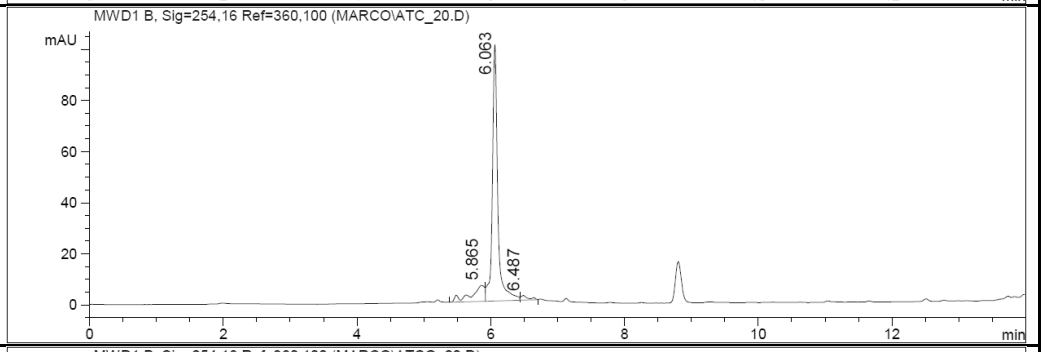
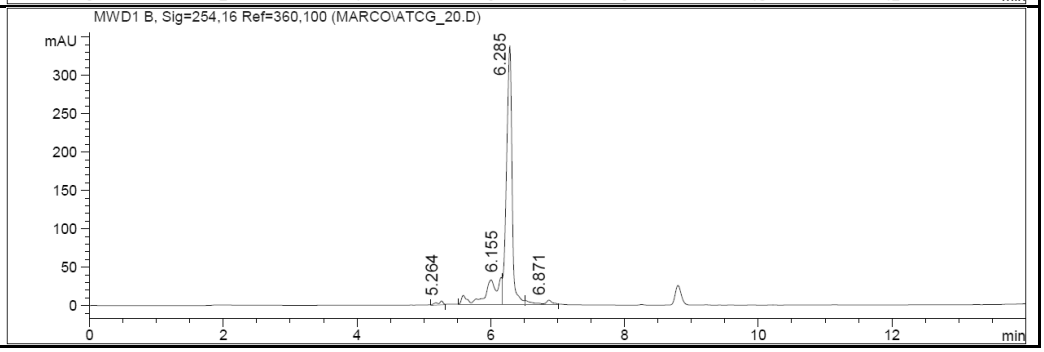
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with Cinchonidine **L** (200 equiv., 4 µmol) in dry MeOH.

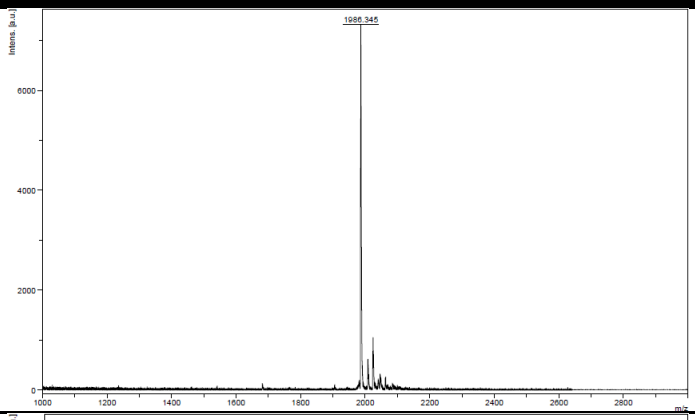
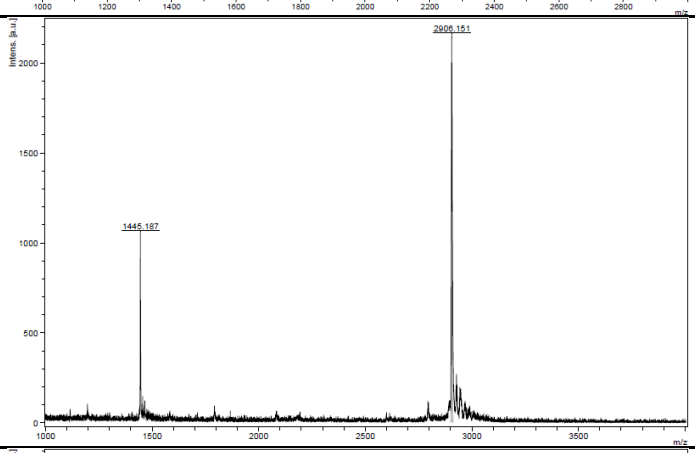
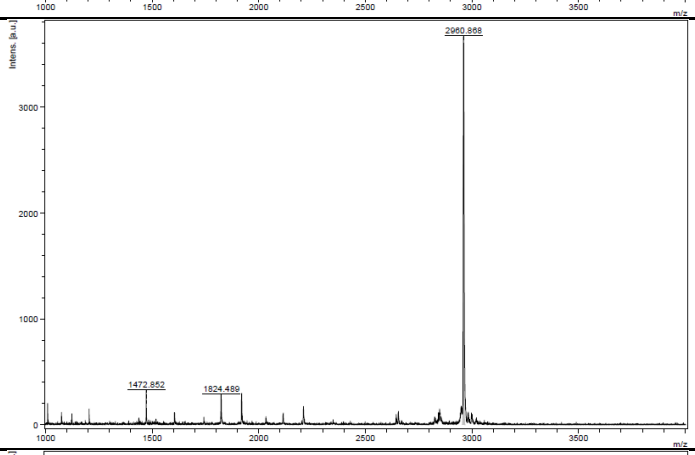
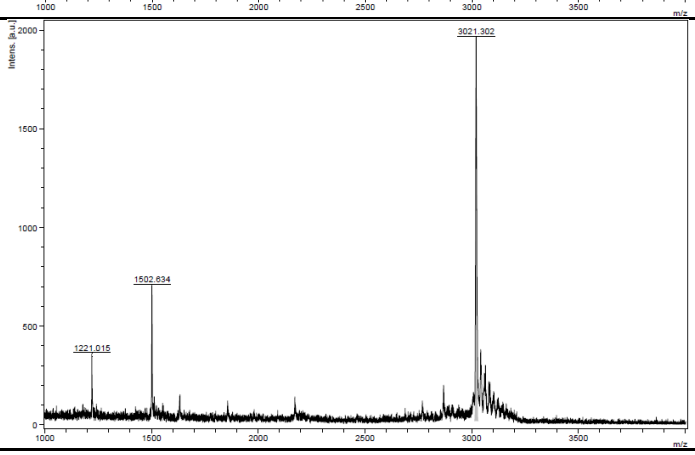
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.6
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.2
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.1

CPG-oligonucleotide + $(DHQD)_2PHAL$ M

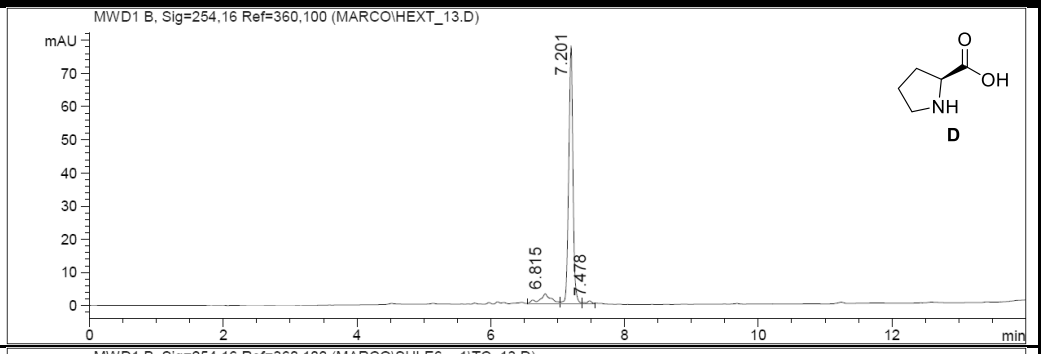
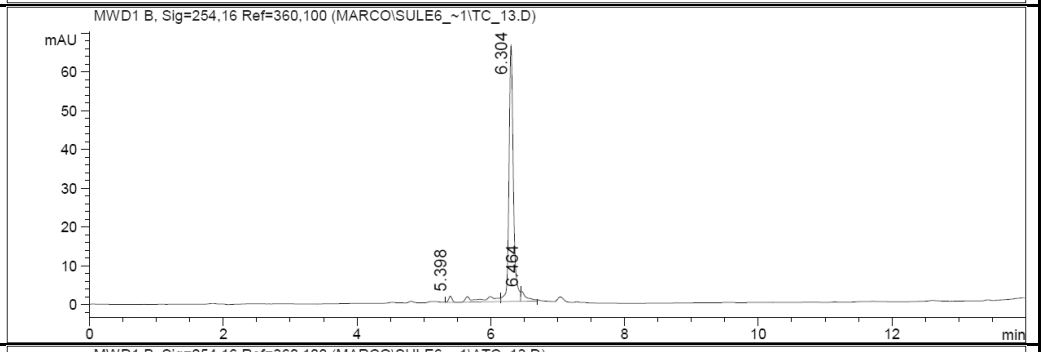
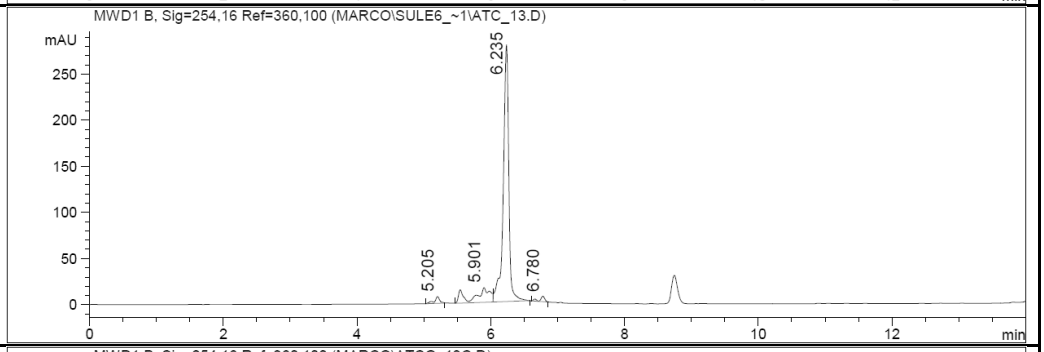
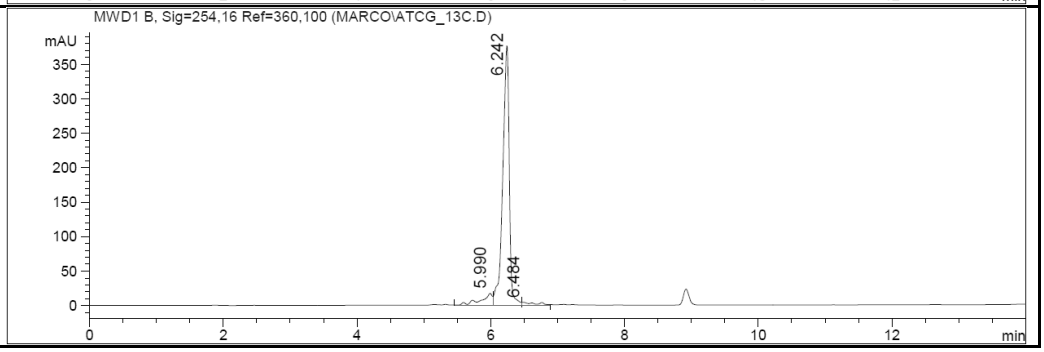
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with $(DHQD)_2PHAL$ **M** (200 equiv., 4 µmol) in dry MeOH.

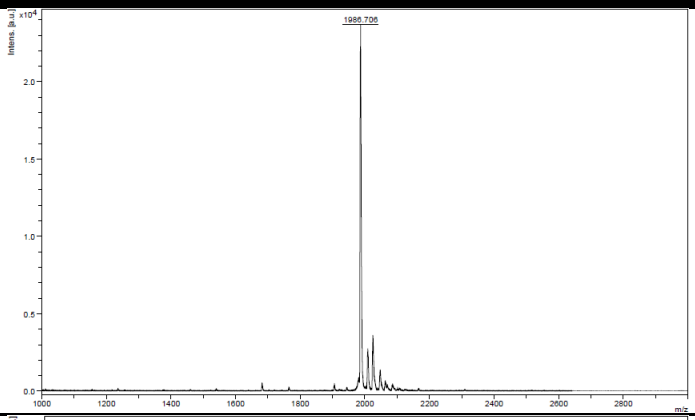
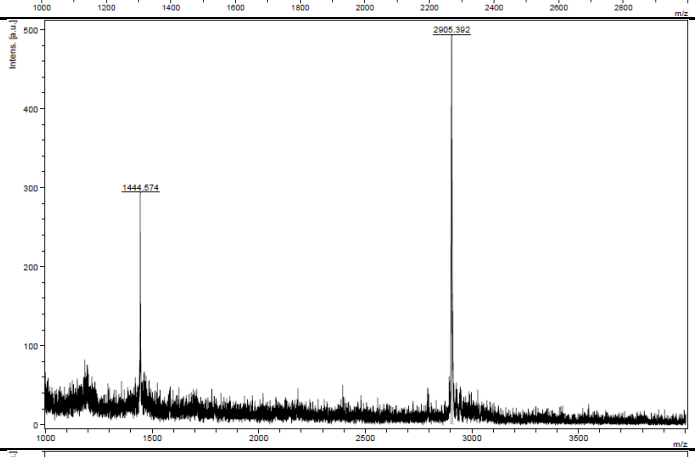
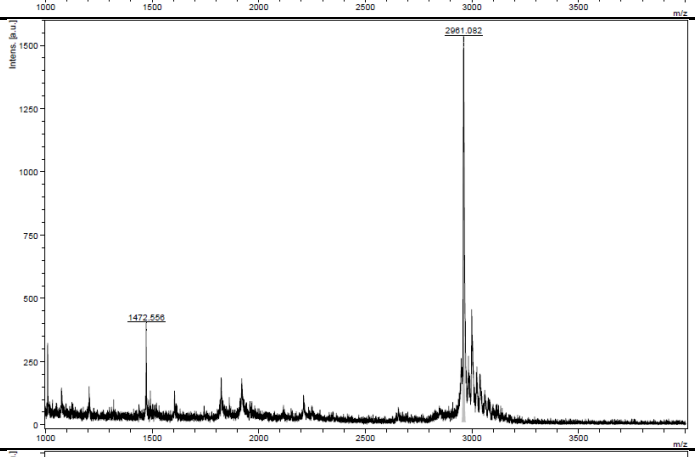
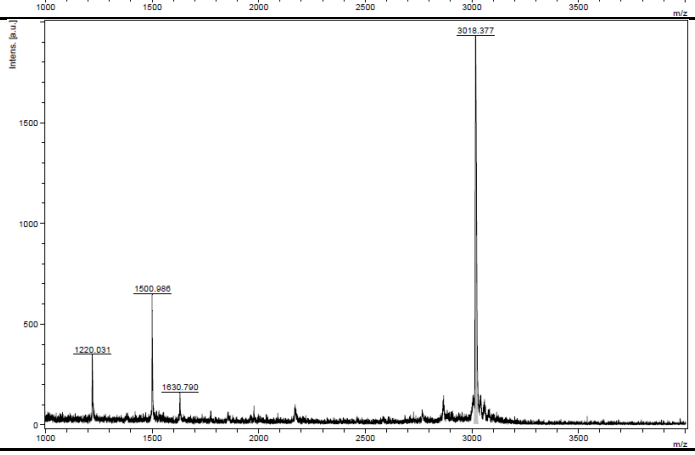
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **$AcNH-(CH_2)_6-$** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.4
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2906.2
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2960.9
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3021.3

CPG-oligonucleotide + L-Prolin D

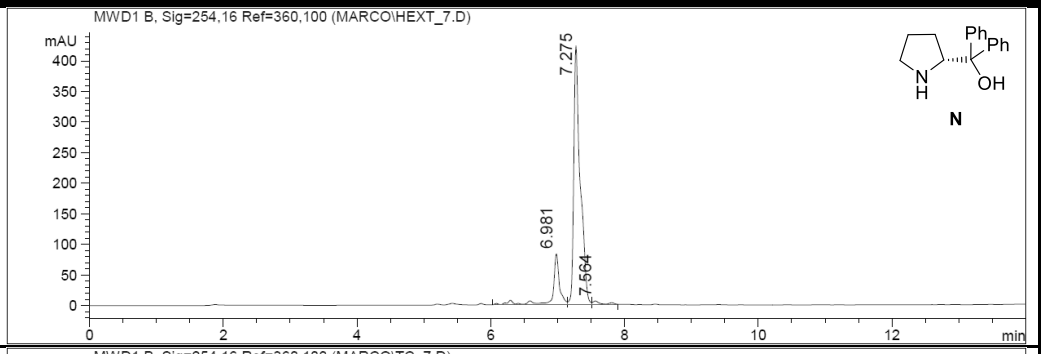
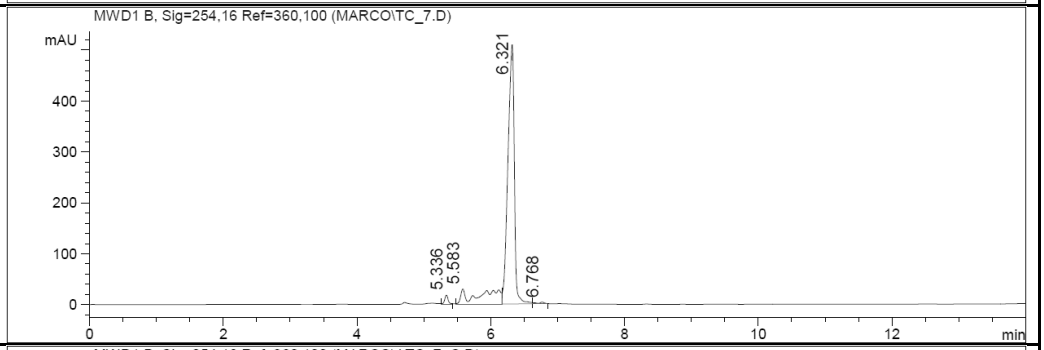
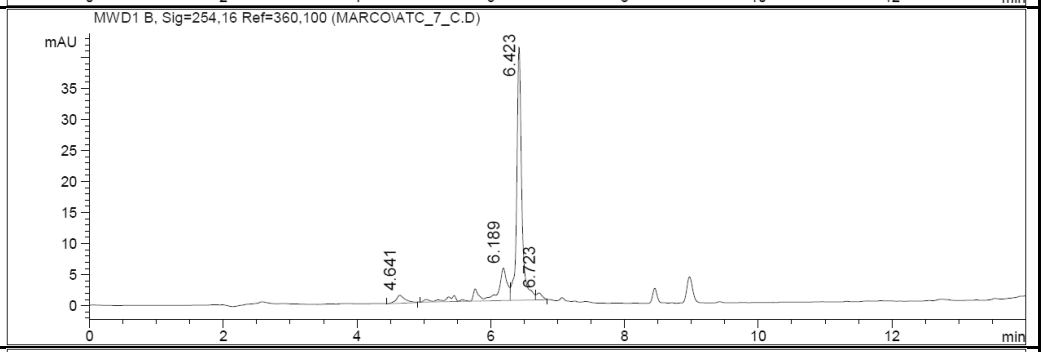
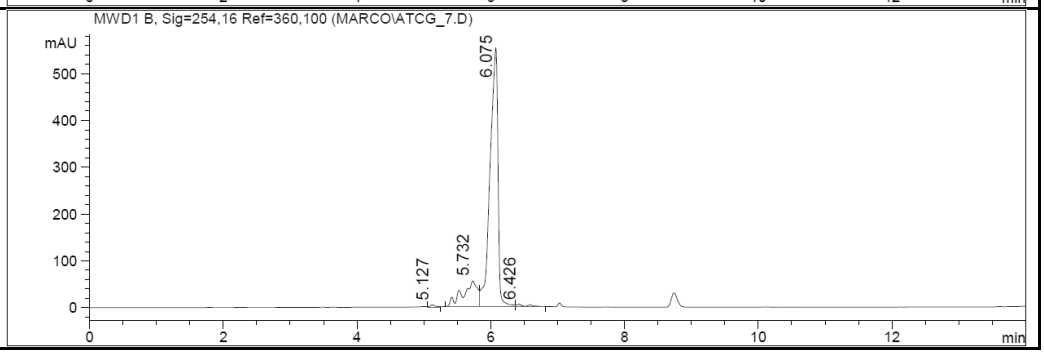
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with L-Prolin **D** (200 equiv., 4 µmol) in dry ACN.

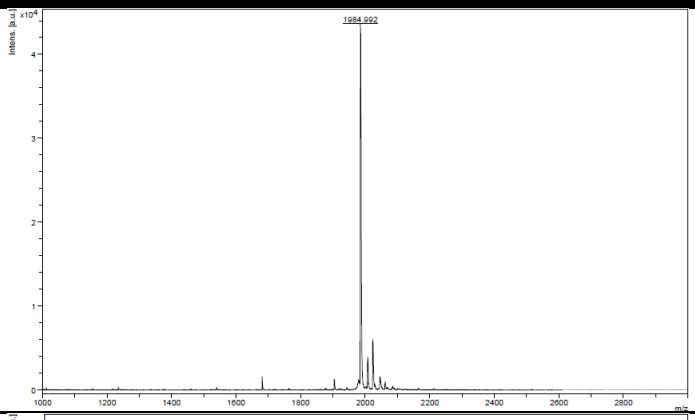
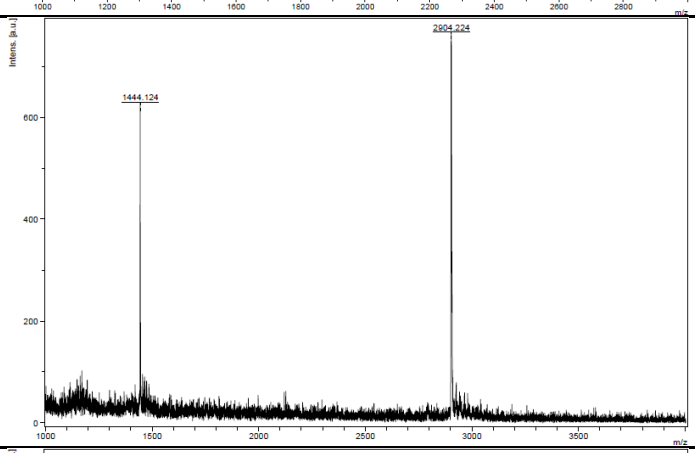
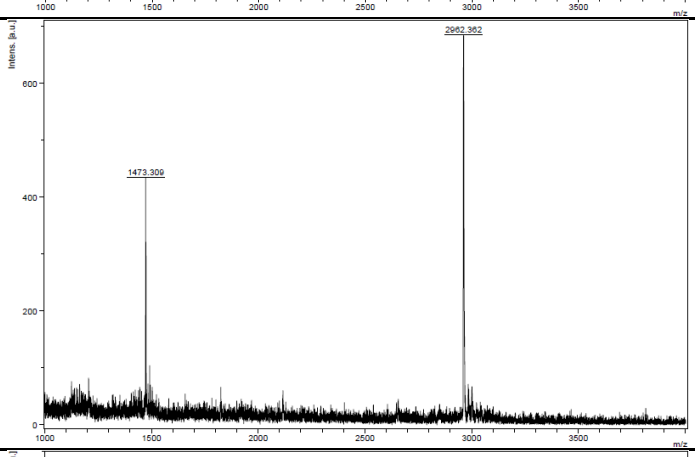
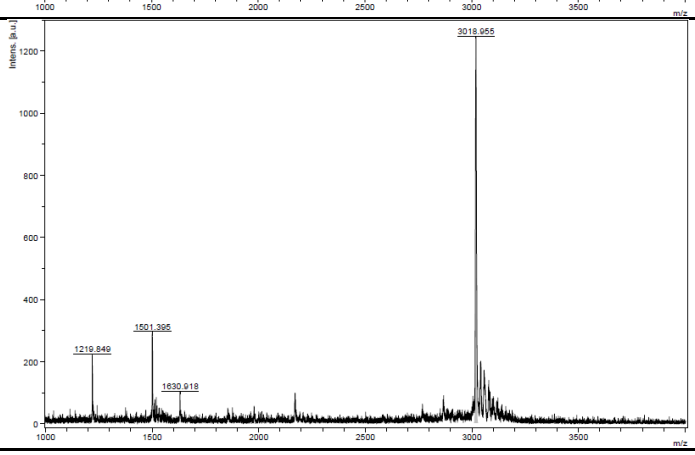
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.7
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.0
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.4

CPG-oligonucleotide + (*R*)-α,α-Diphenylprolinol N

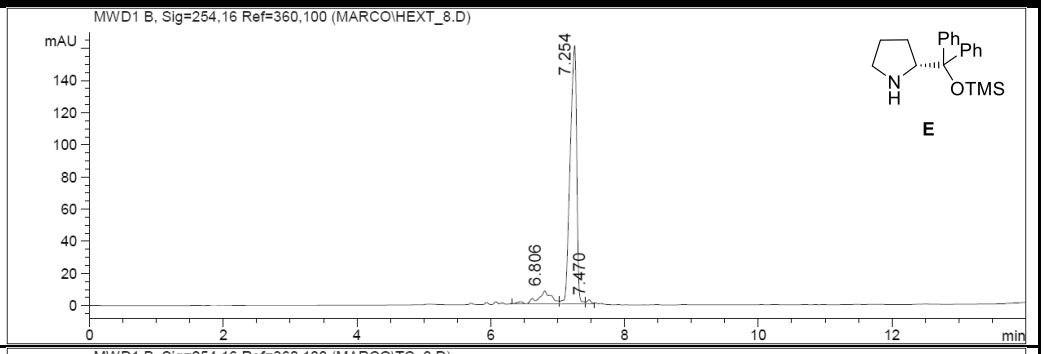
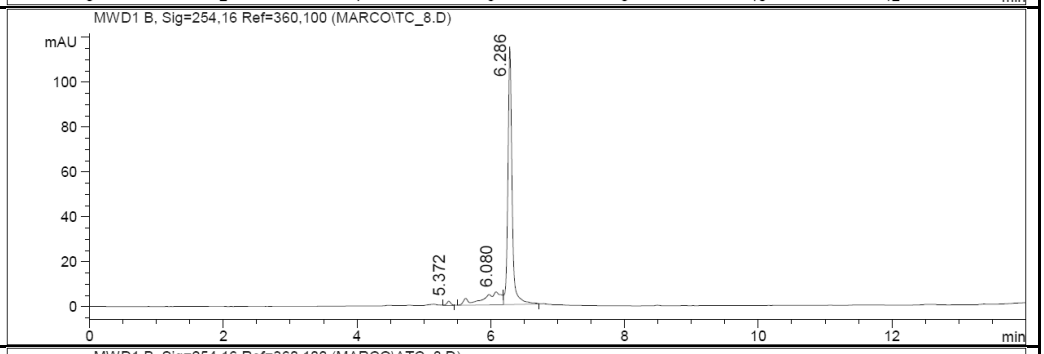
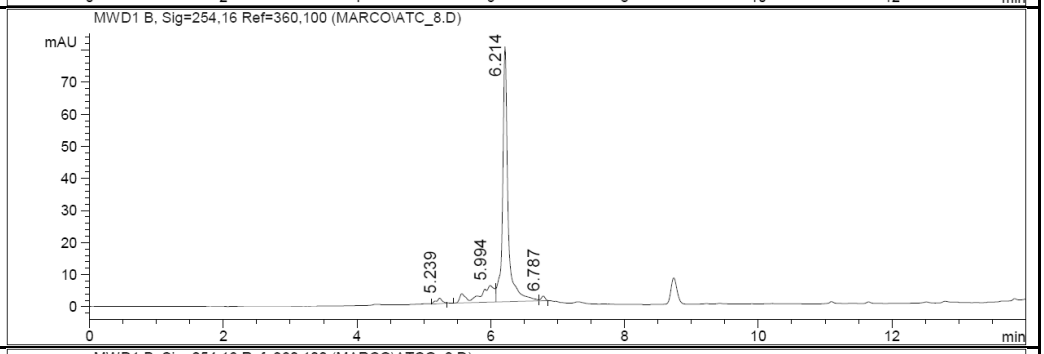
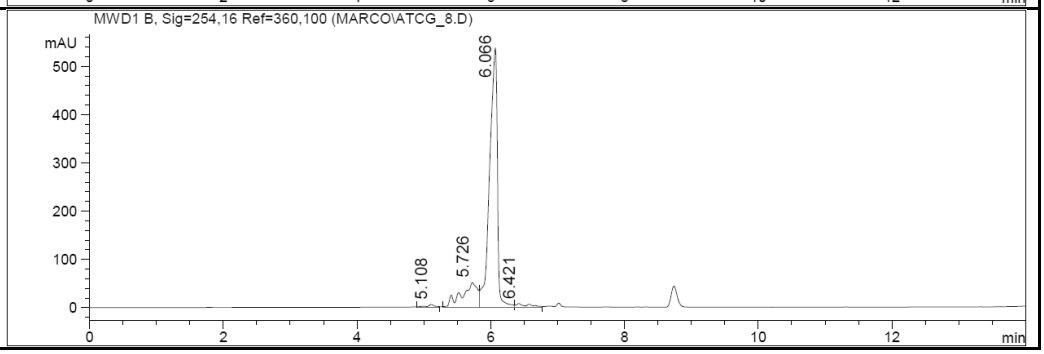
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (*R*)-α,α-Diphenylprolinol **N** (200 equiv., 4 µmol) in dry ACN.

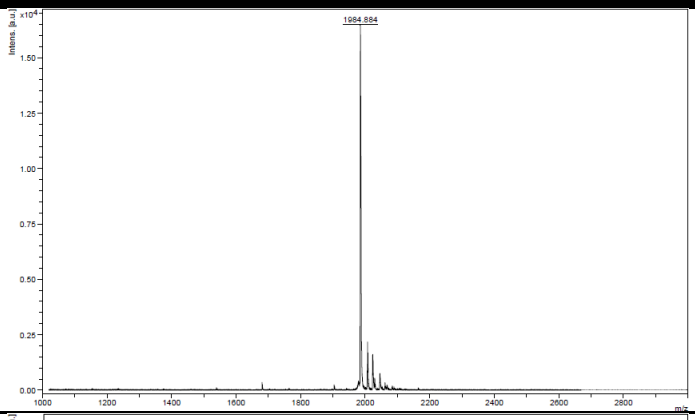
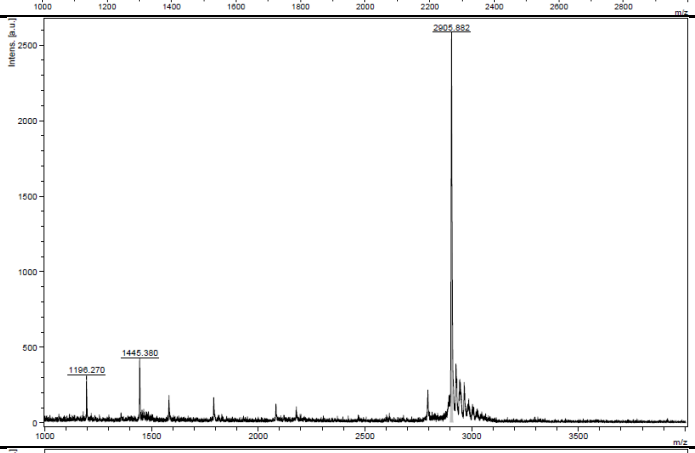
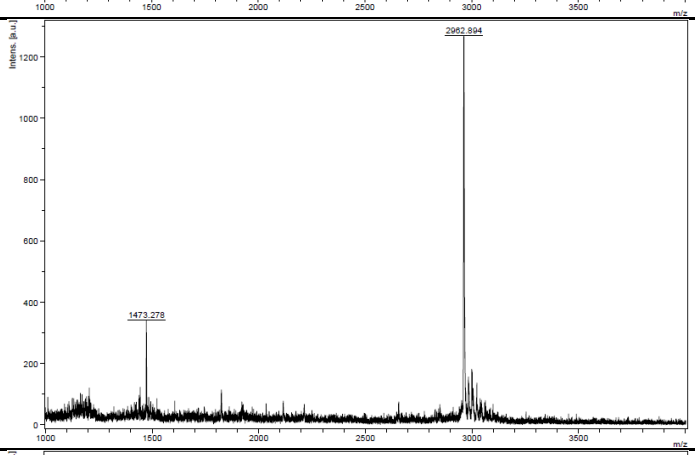
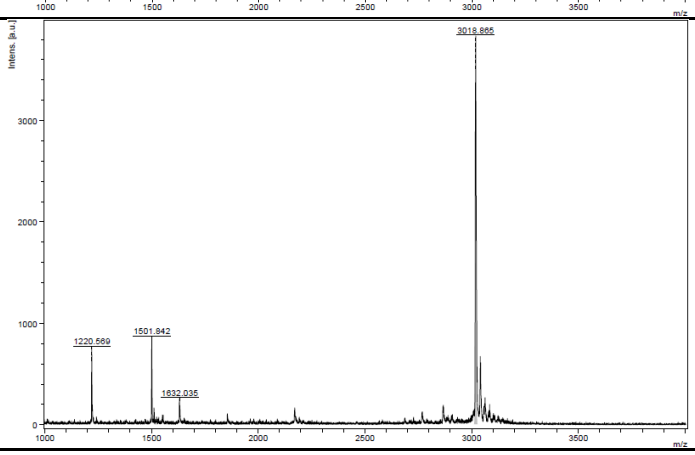
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.2
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.4
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.0

CPG-oligonucleotide + (*R*)-α,α-Diphenylprolinol TMS ether E

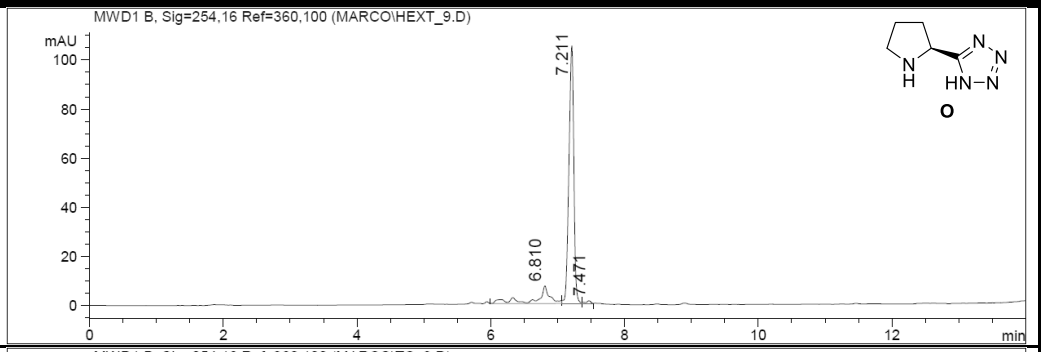
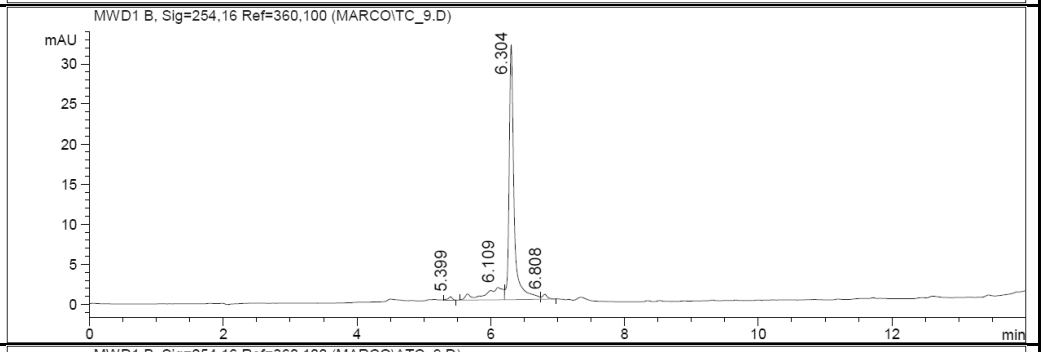
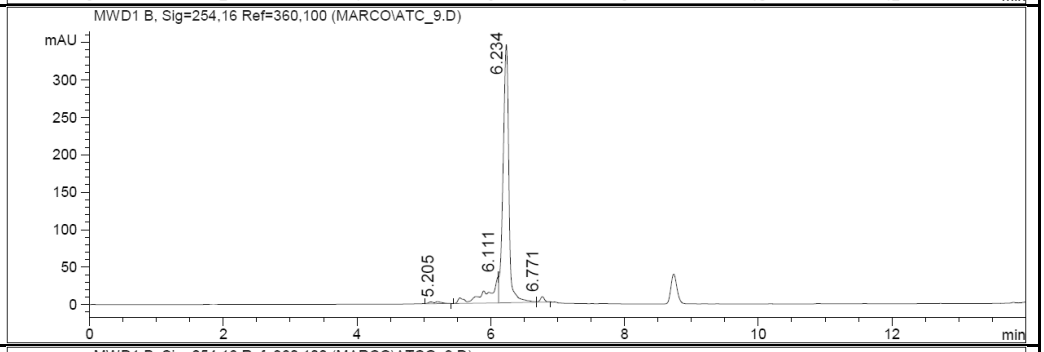
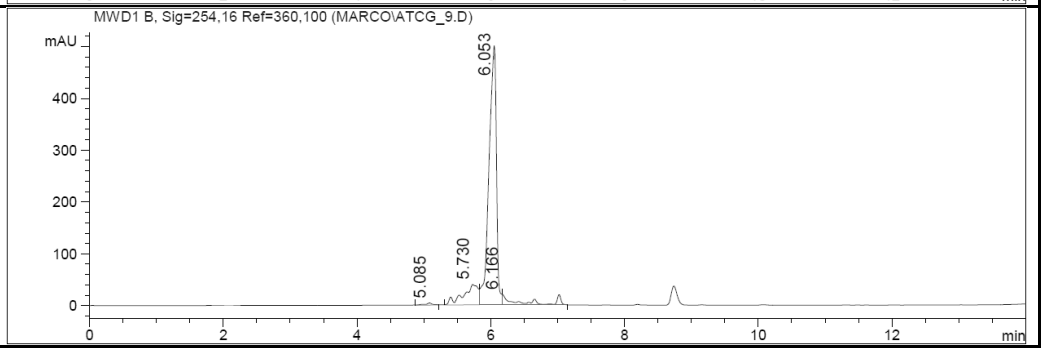
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (*R*)-α,α-Diphenylprolinol TMS ether **E** (200 equiv., 4 µmol) in dry ACN.

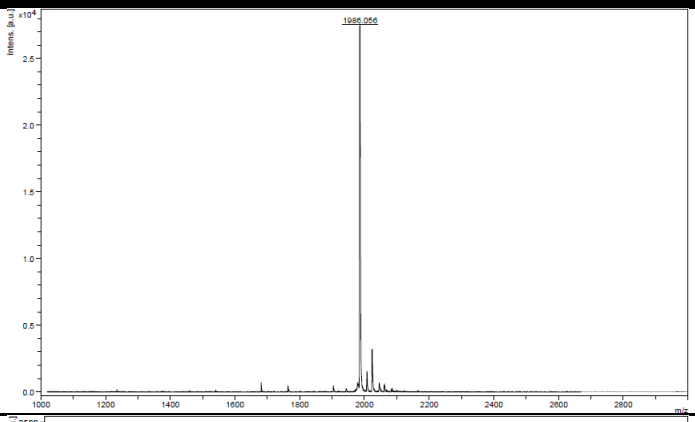
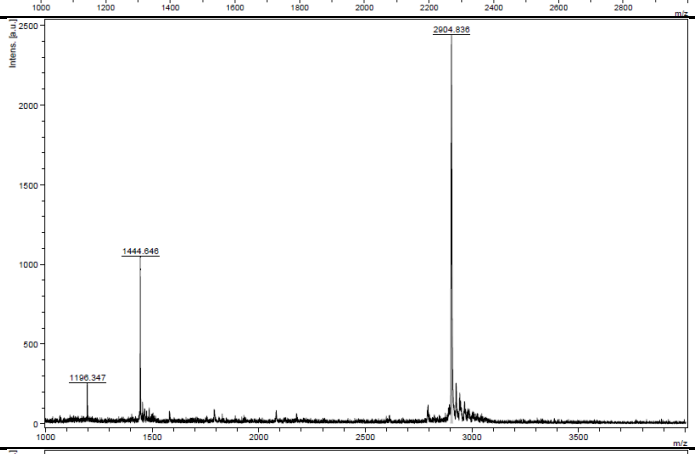
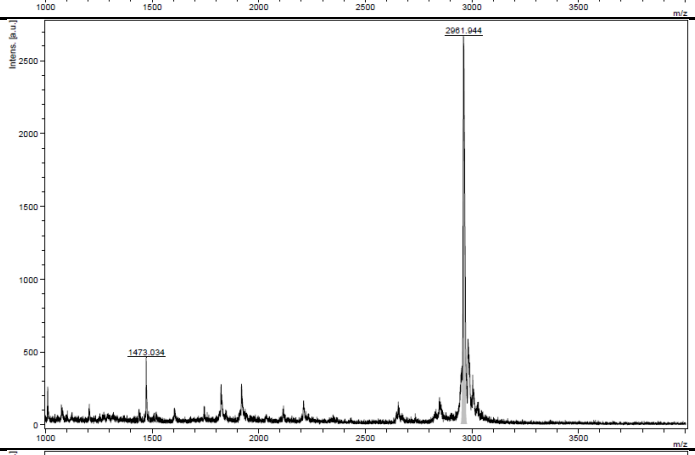
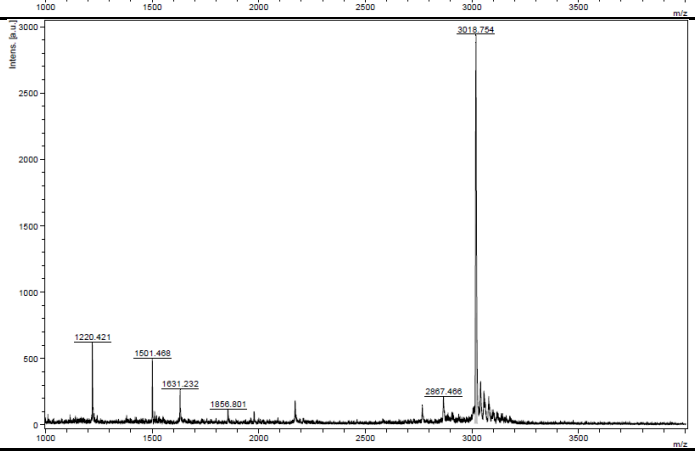
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1984.9
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.9
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.9

CPG-oligonucleotide + (*S*)-(-)-2-Tetrazol-5-ylpyrrolidine O

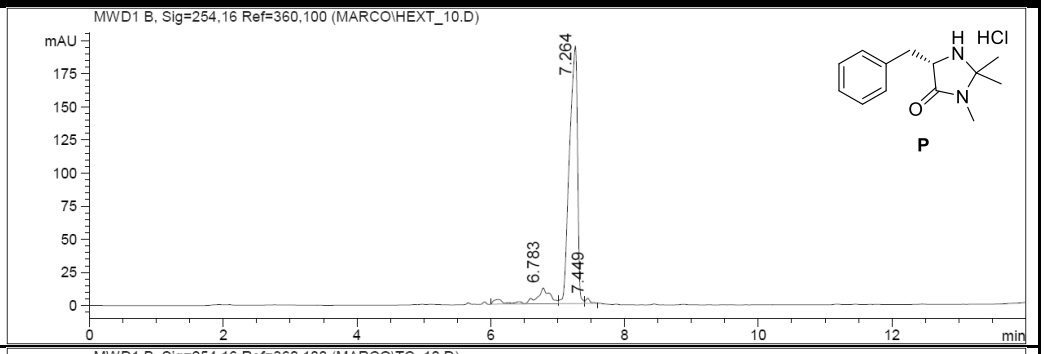
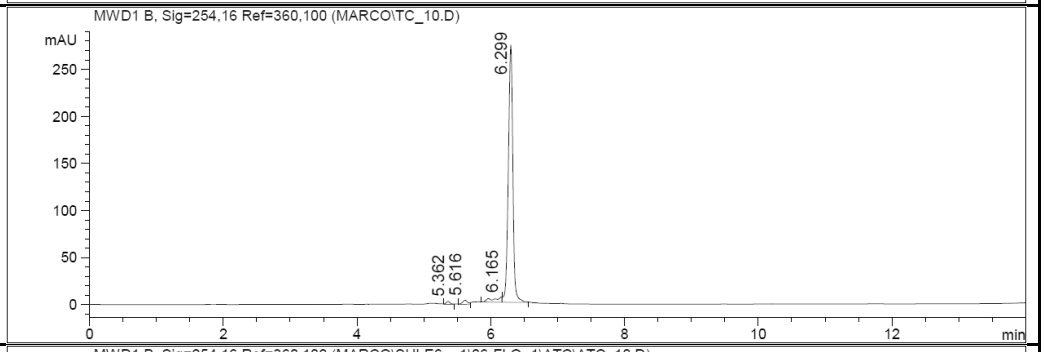
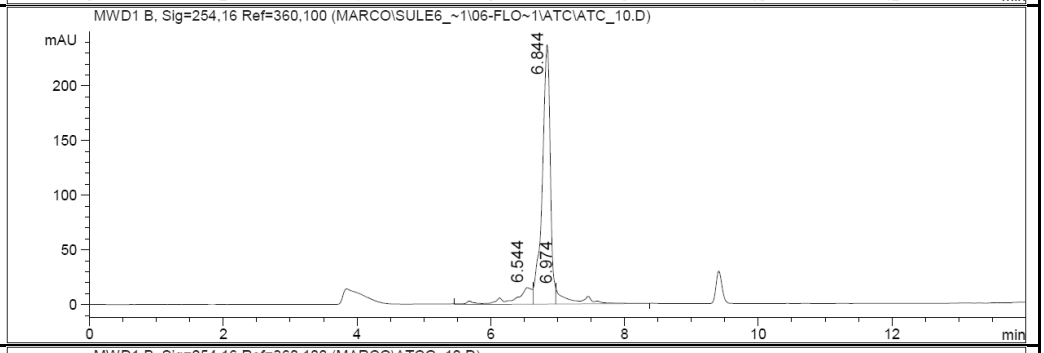
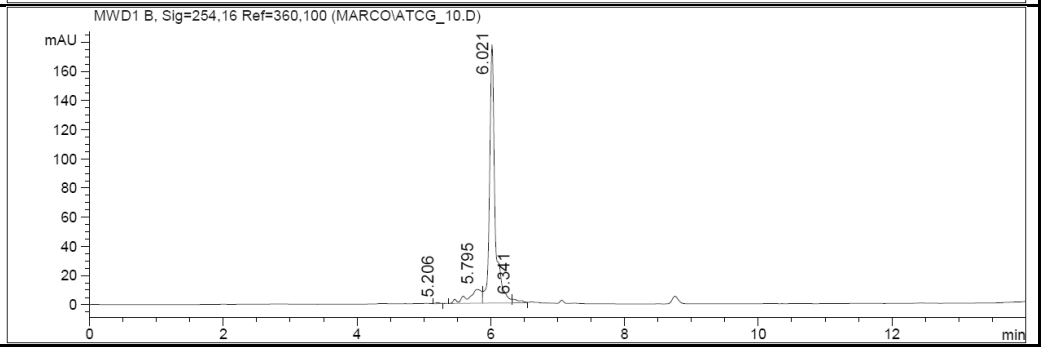
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (*S*)-(-)-2-Tetrazol-5-ylpyrrolidine **O** (200 equiv., 4 µmol) in dry MeOH.

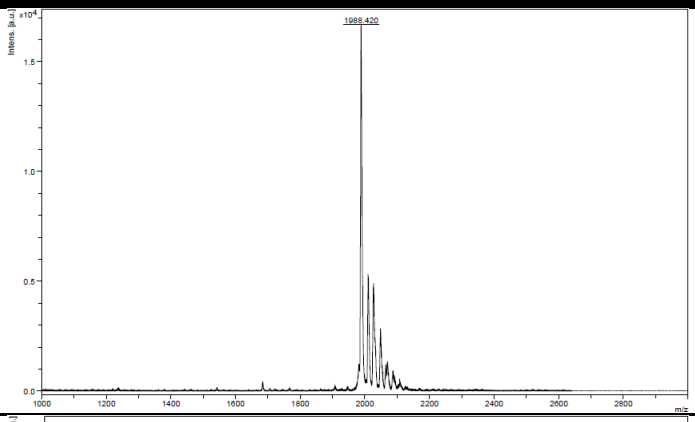
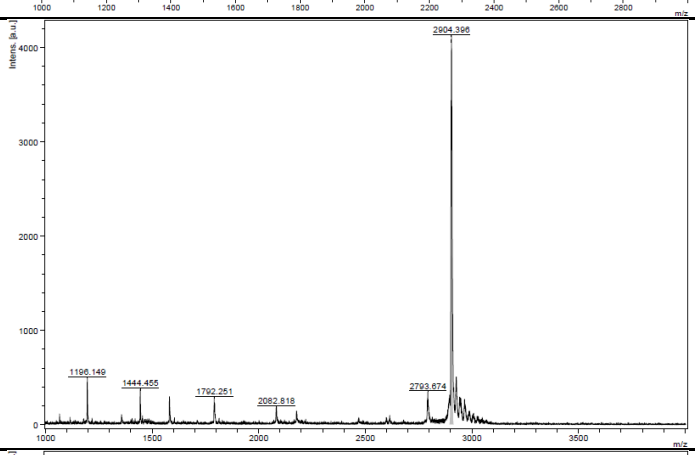
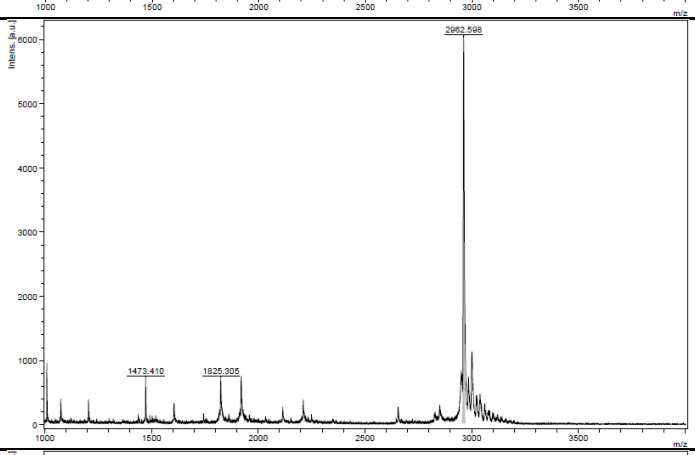
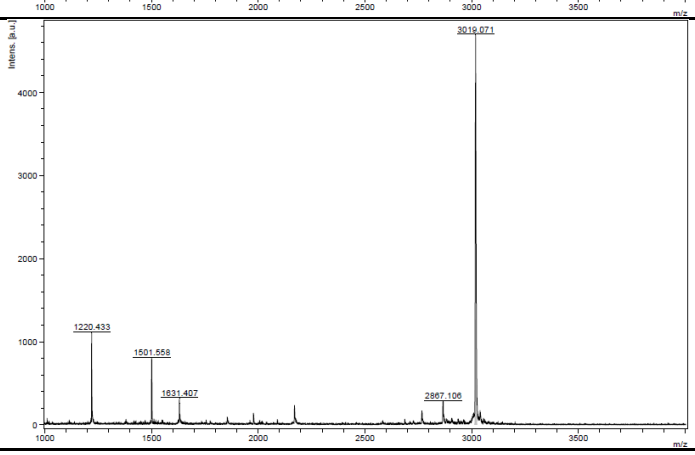
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.1
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.8
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.9
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.8

CPG-oligonucleotide + (5*S*)-(-)-2,2,3-Trimethyl-5-benzyl-4-imidazolidinone monohydrochloride P

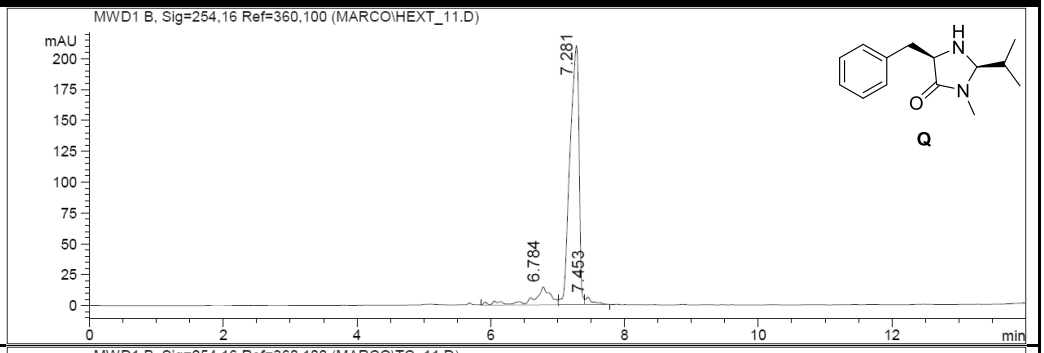
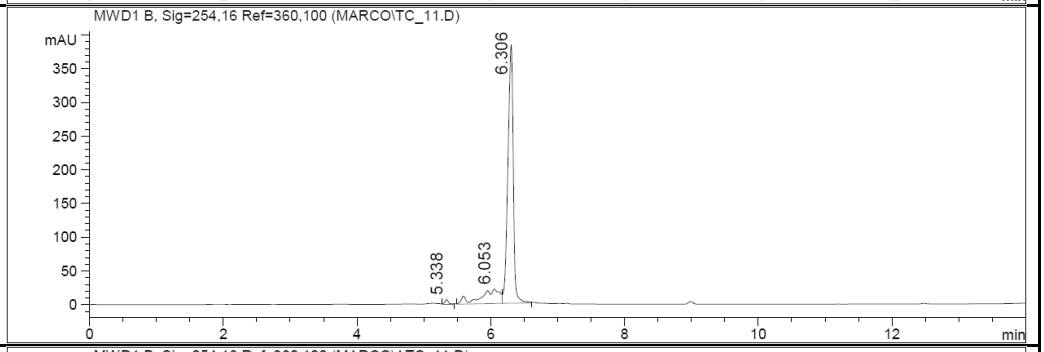
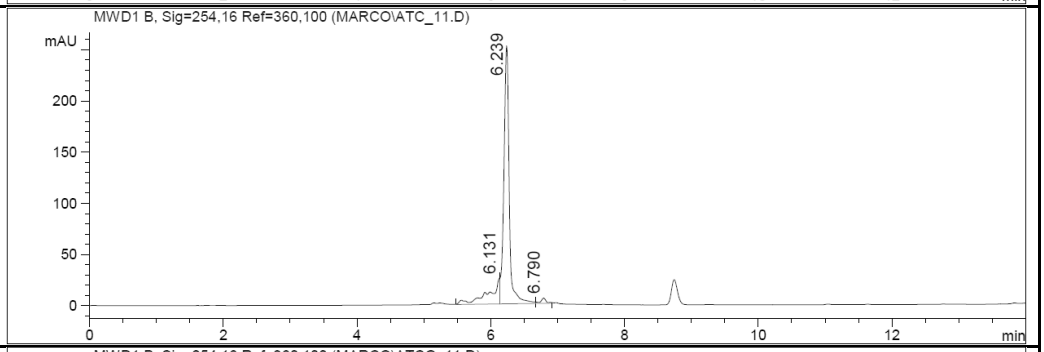
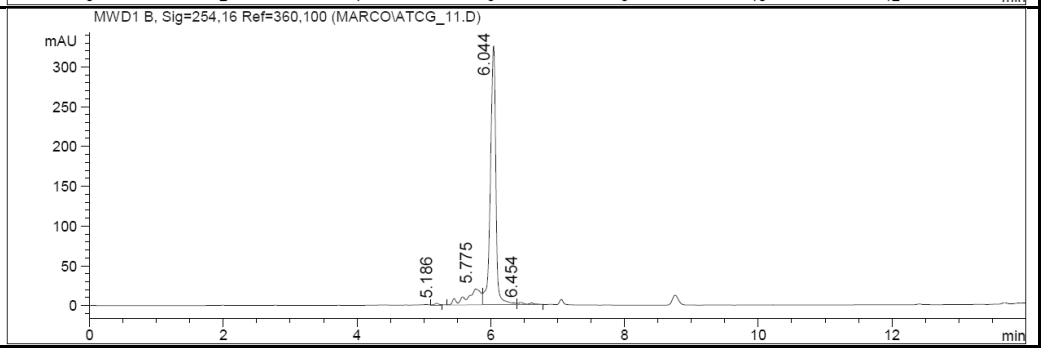
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (5*S*)-(-)-2,2,3-Trimethyl-5-benzyl-4-imidazolidinone monohydrochloride **P** (200 equiv., 4 µmol) in dry MeOH.

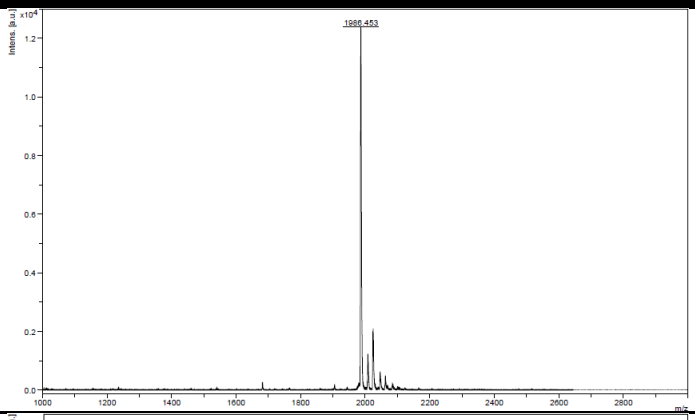
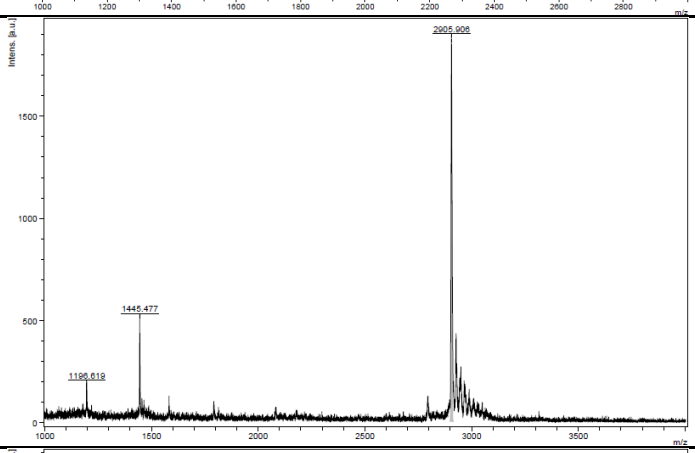
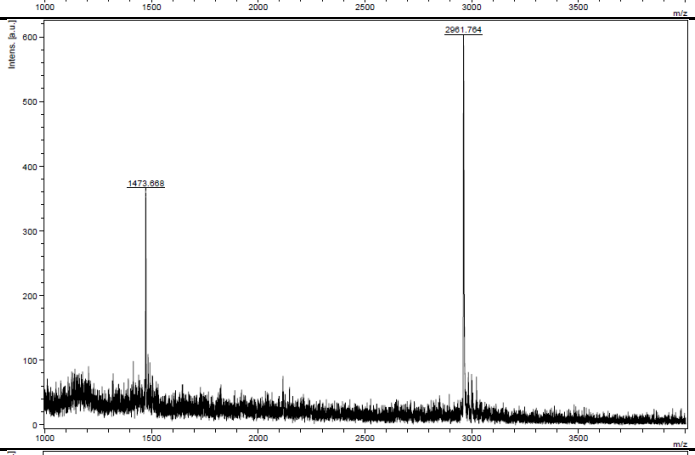
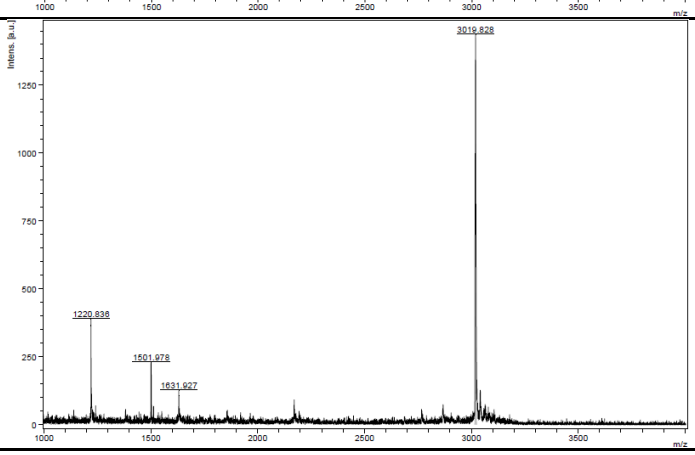
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1988.4
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.6
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.1

CPG-oligonucleotide + (2*R*,5*R*)-(+)-2-*tert*-Butyl-3-methyl-5-benzyl-4-imidazolidinone Q

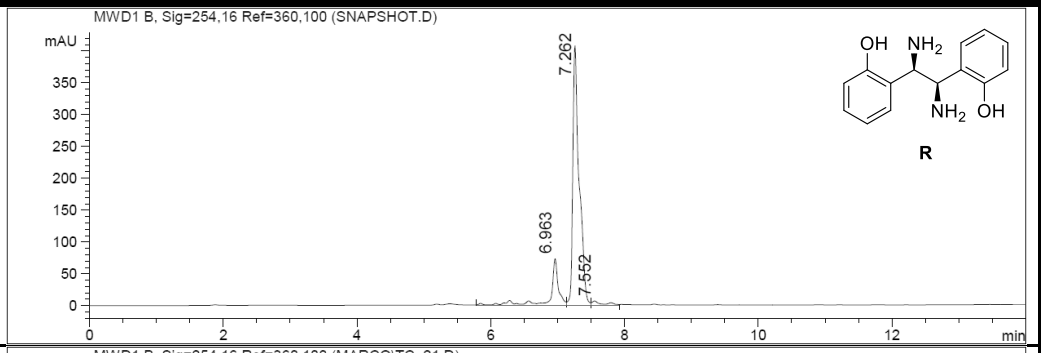
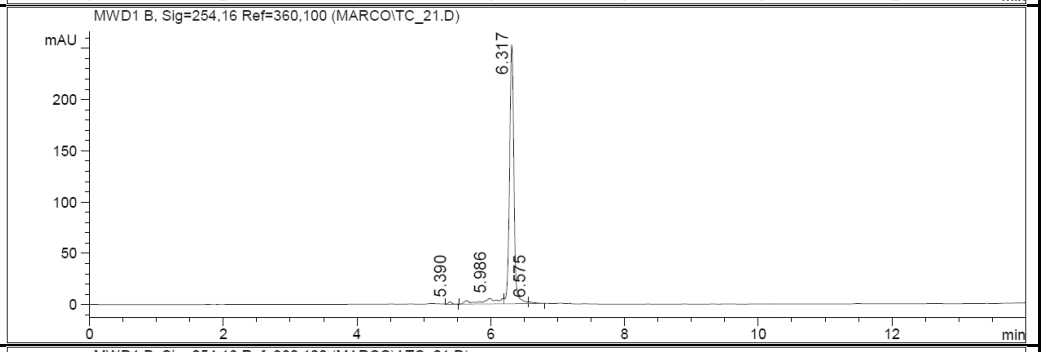
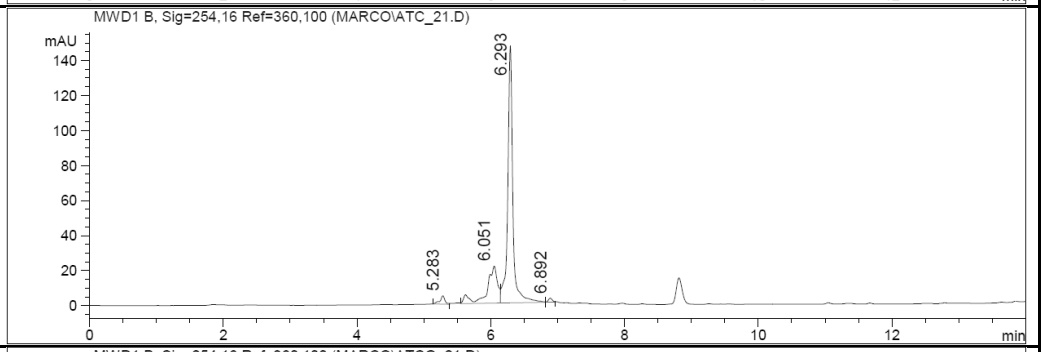
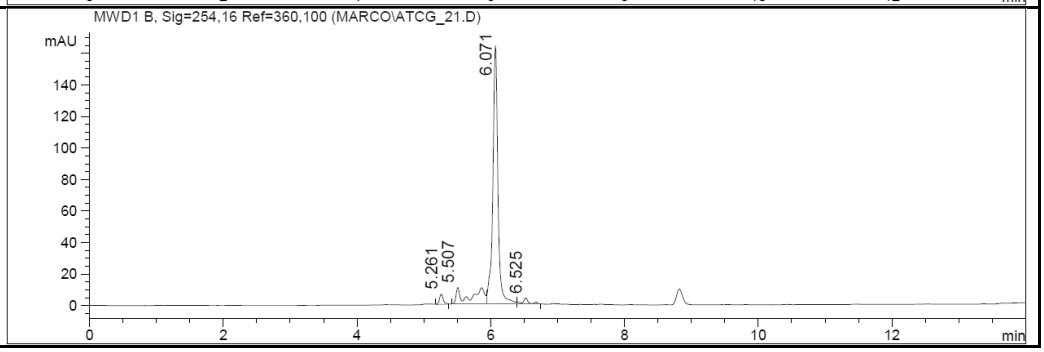
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (2*R*,5*R*)-(+)-2-*tert*-Butyl-3-methyl-5-benzyl-4-imidazolidinone **Q** (200 equiv., 4 µmol) in dry ACN.

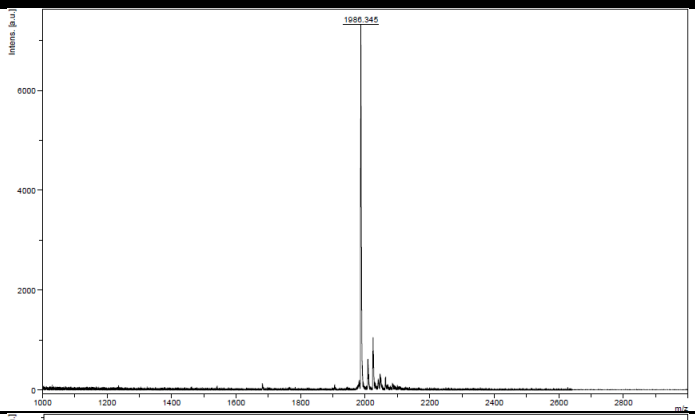
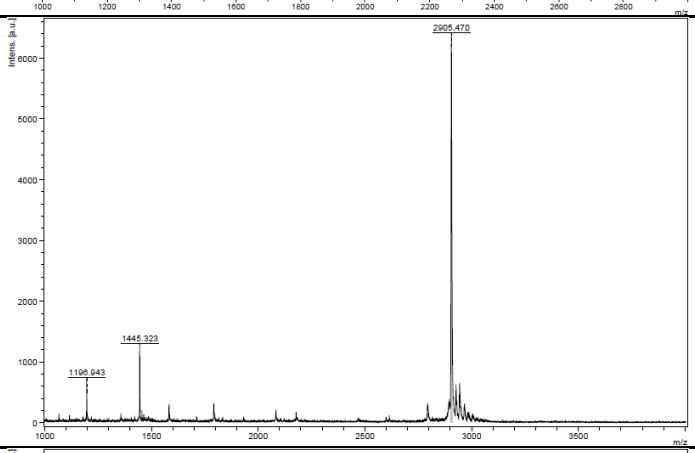
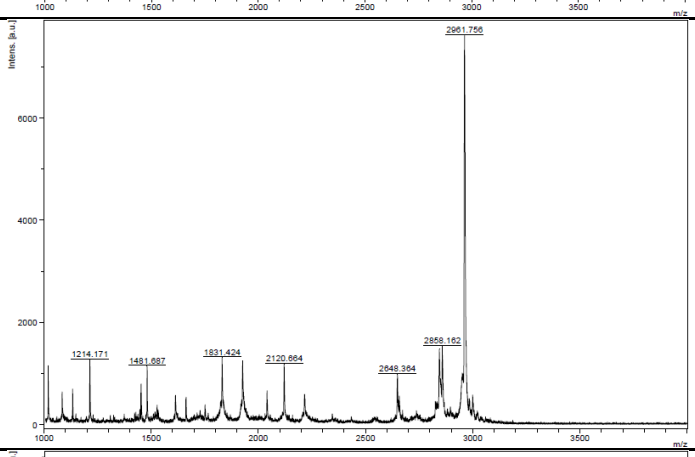
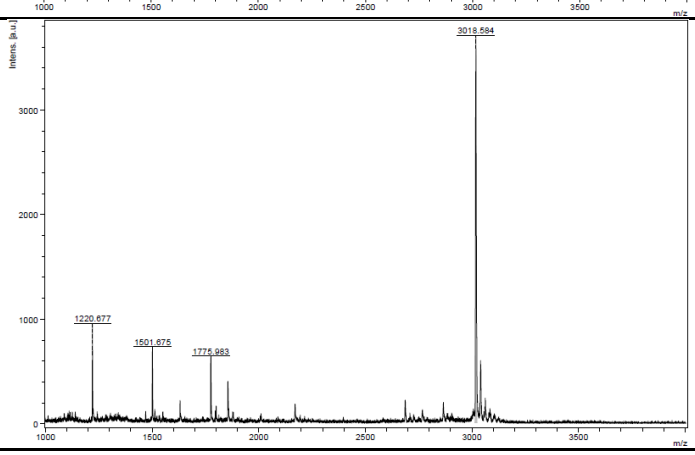
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.5
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.9
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3019.8

CPG-oligonucleotide + (1*R*,2*R*)-1,2-Bis(2-hydroxyphenyl)ethylenediamine R

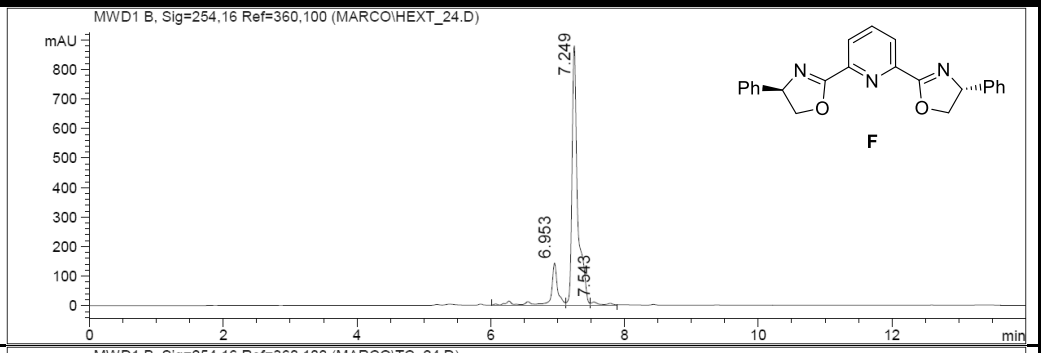
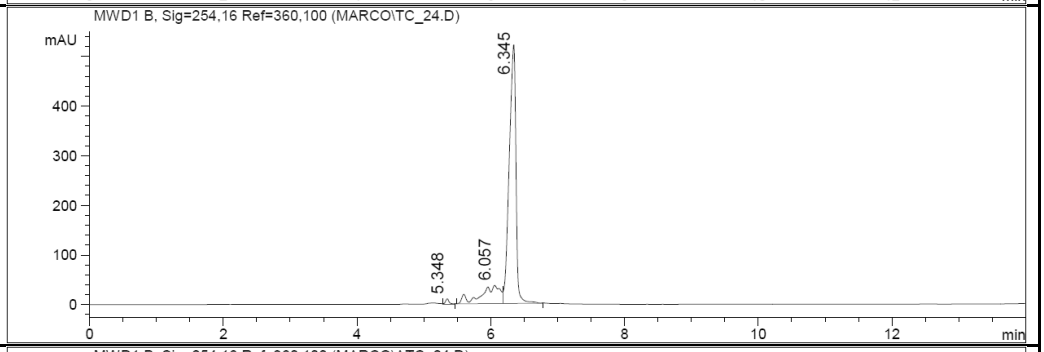
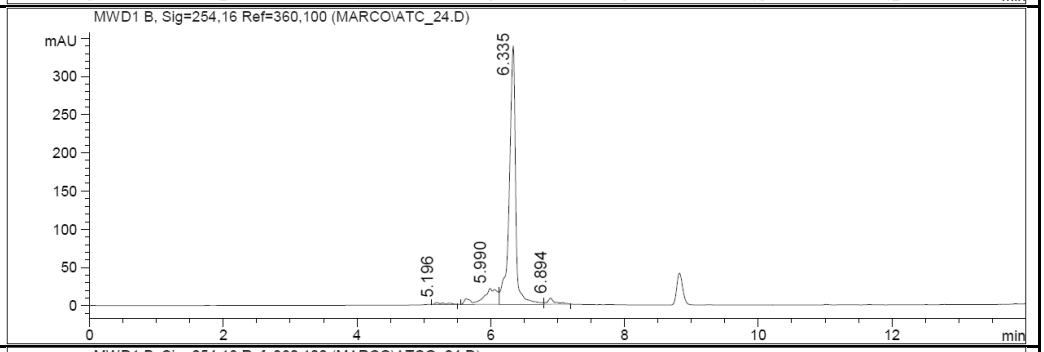
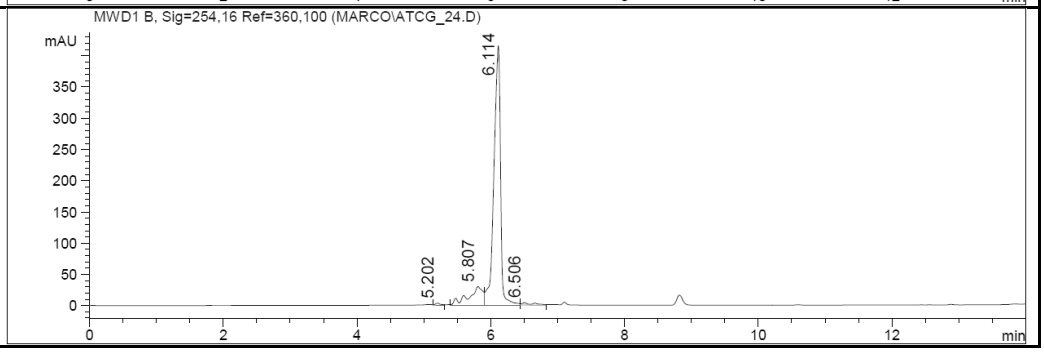
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (1*R*,2*R*)-1,2-Bis(2-hydroxyphenyl)ethylenediamine **R** (200 equiv., 4 µmol) in dry MeOH.

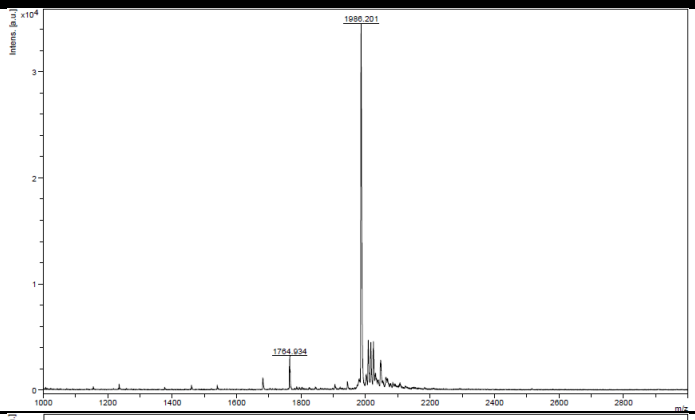
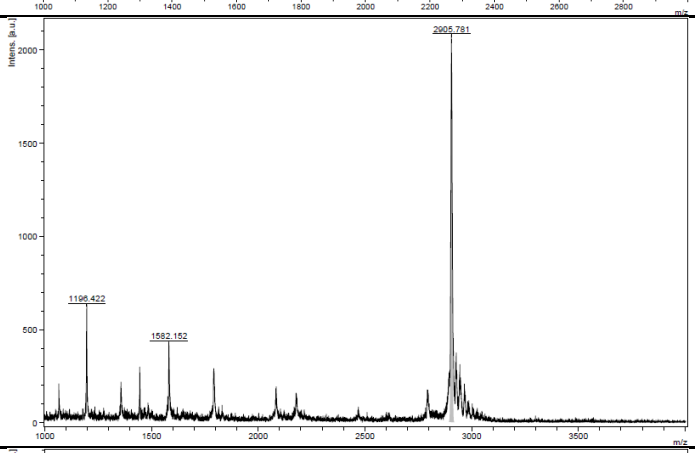
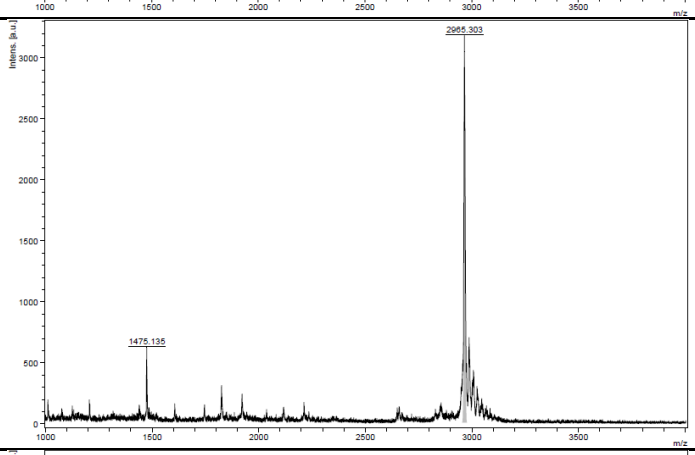
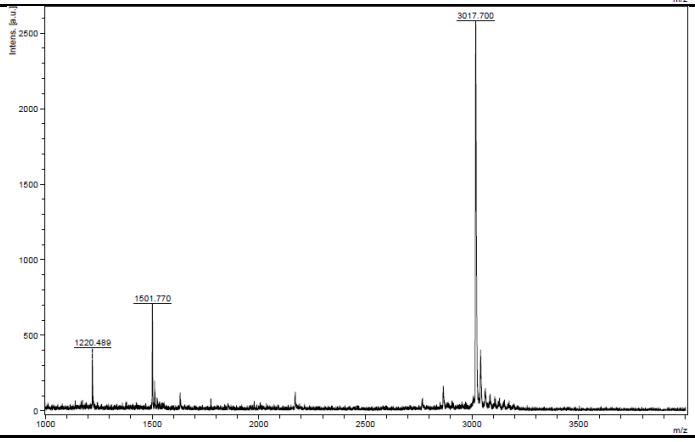
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.3
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.5
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.6

CPG-oligonucleotide + (*R*,*R*)-2,6-Bis(4-phenyl-2-oxazolin-2-yl)pyridine F

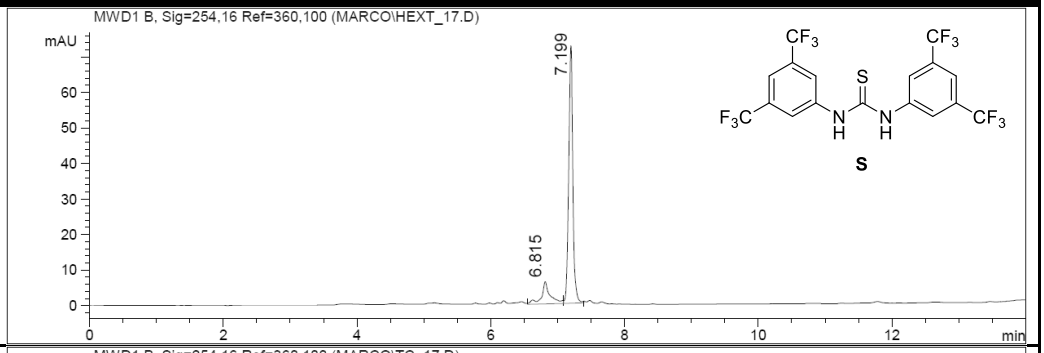
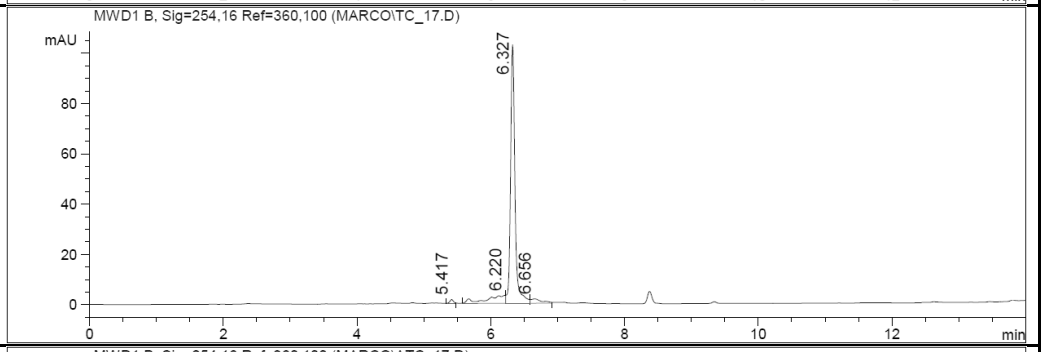
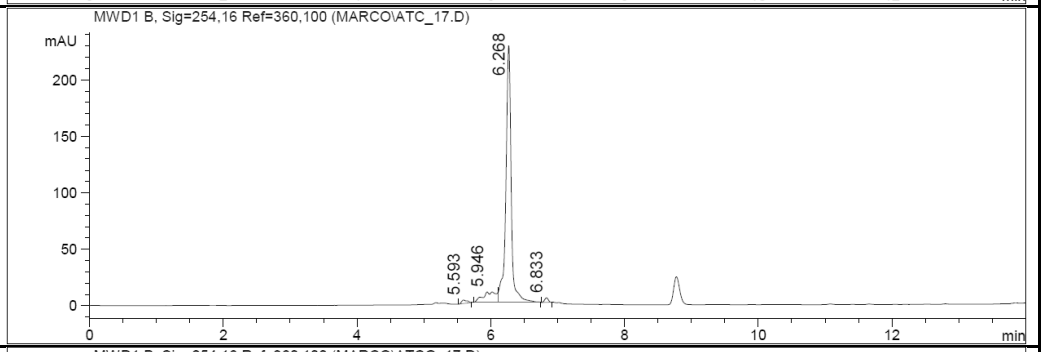
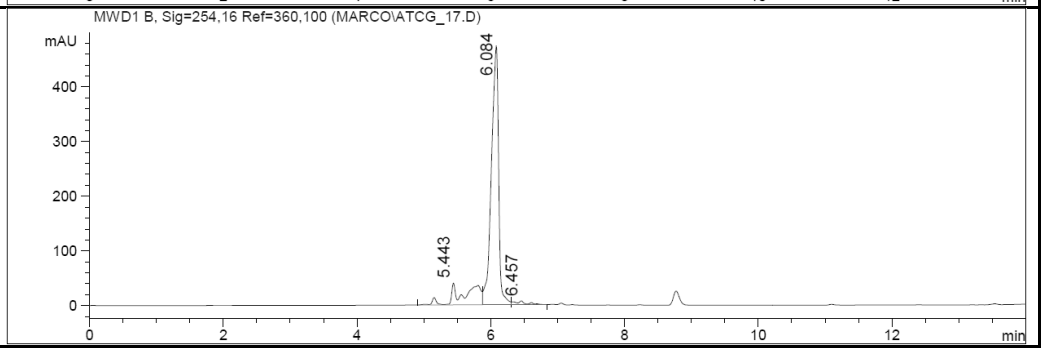
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (*R*,*R*)-2,6-Bis(4-phenyl-2-oxazolin-2-yl)pyridine **F** (200 equiv., 4 µmol) in dry ACN.

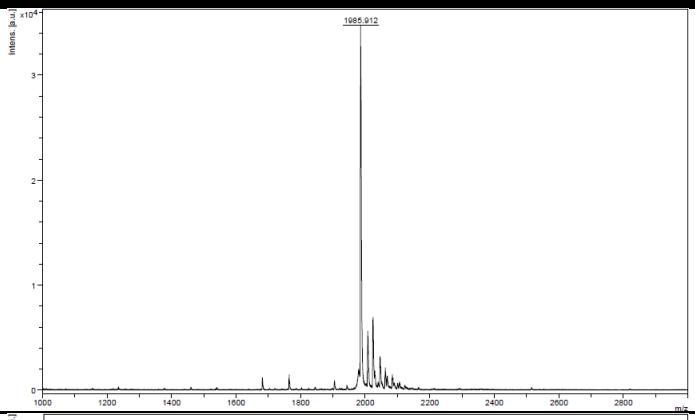
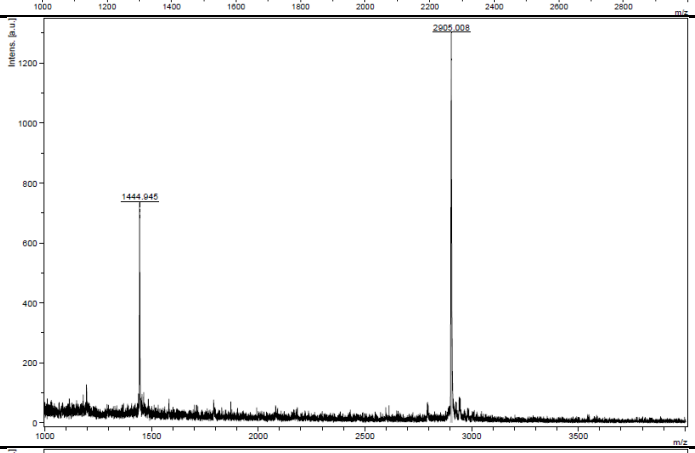
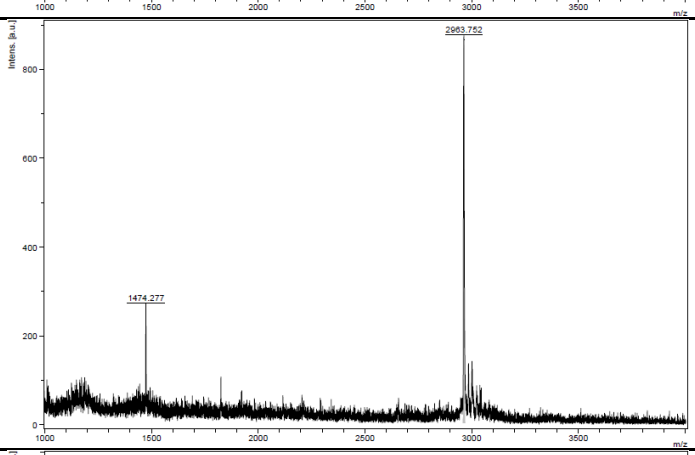
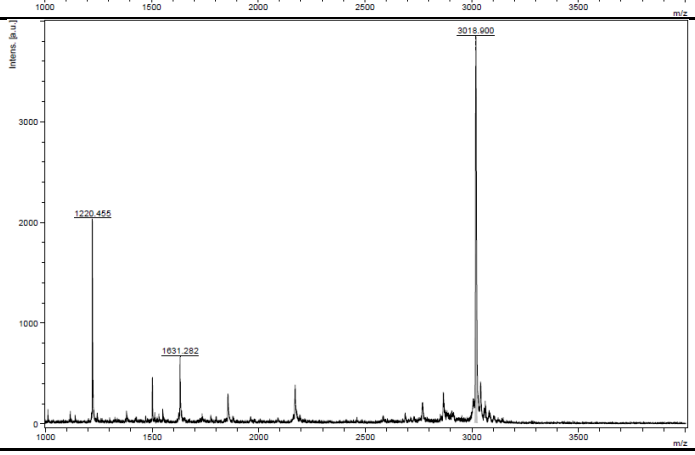
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1986.2
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.8
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2965.3
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.7

CPG-oligonucleotide + *N,N*-bis[3,5-bis(trifluoromethyl)phenyl]-thiourea S

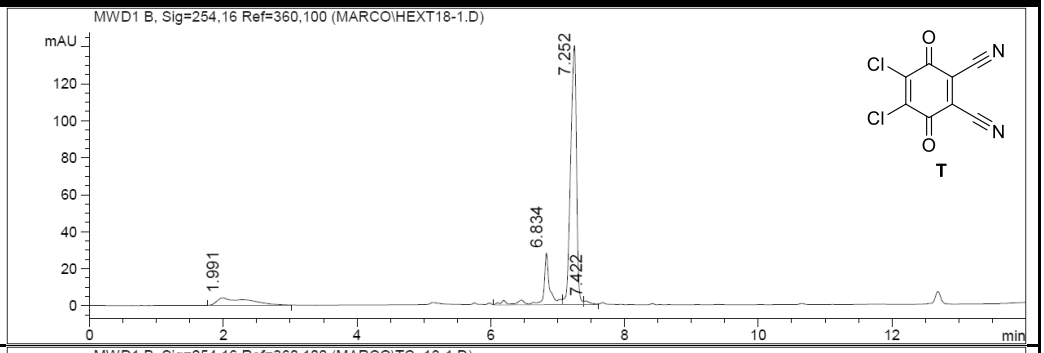
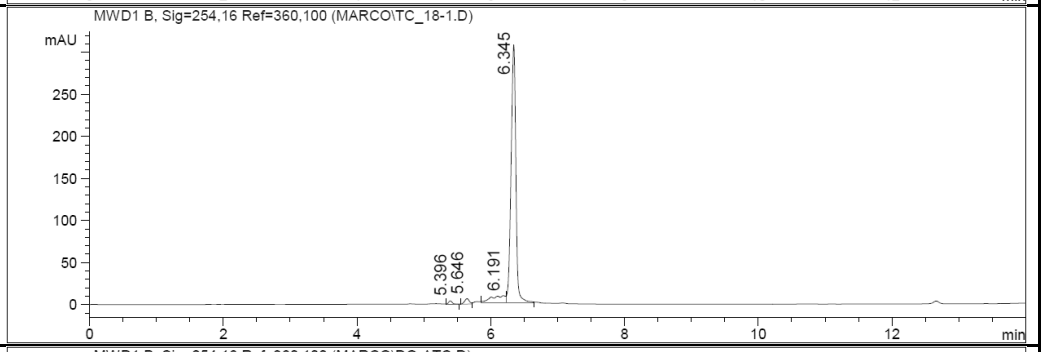
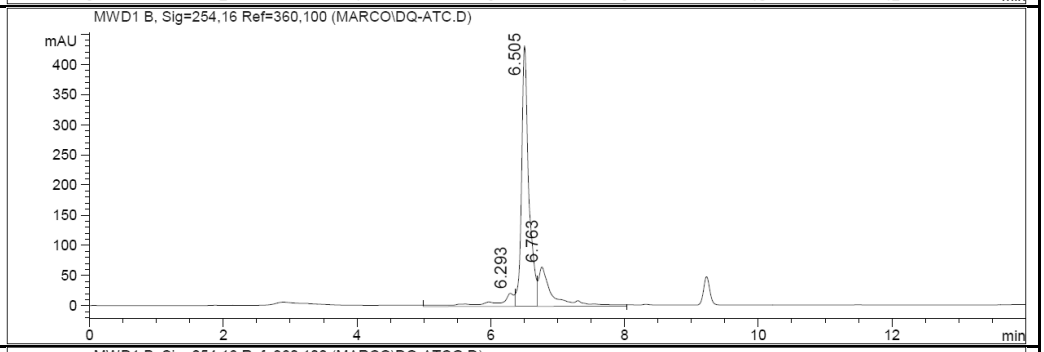
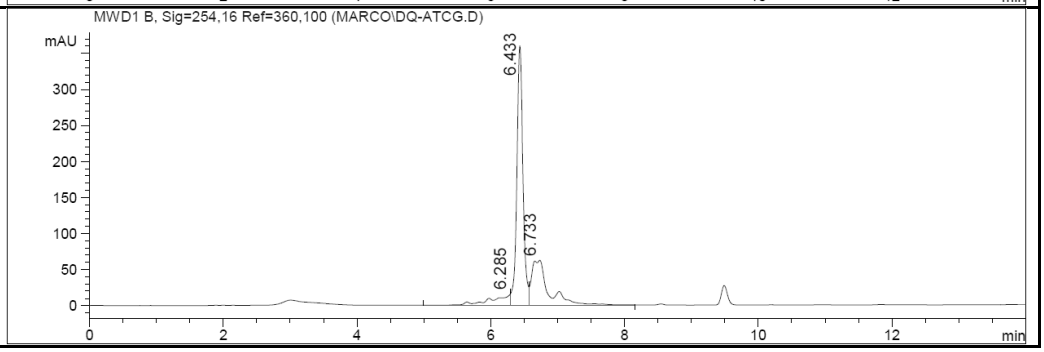
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with *N,N*-bis[3,5-bis(trifluoromethyl)phenyl]-thiourea **S** (200 equiv., 4 µmol) in dry MeOH.

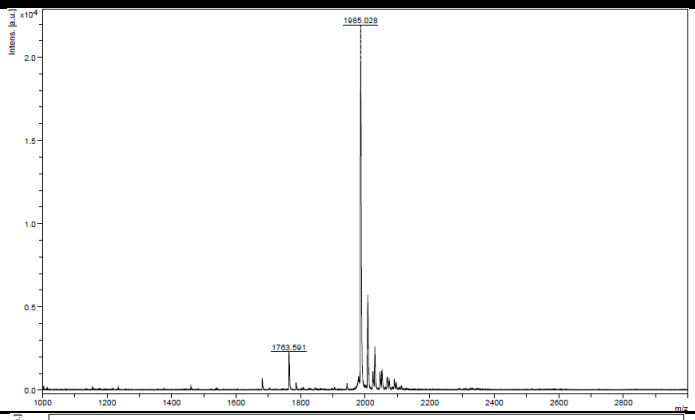
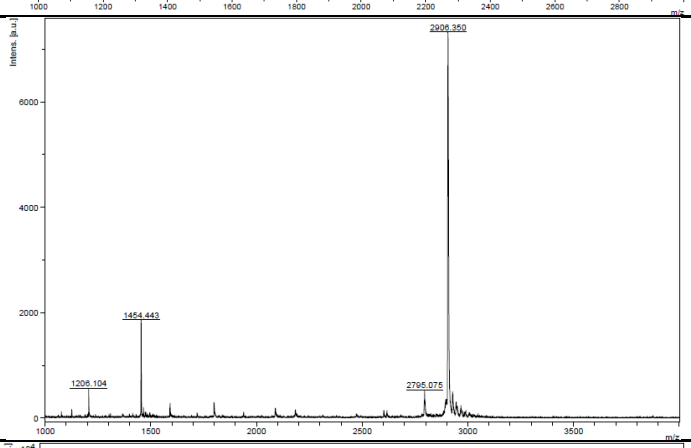
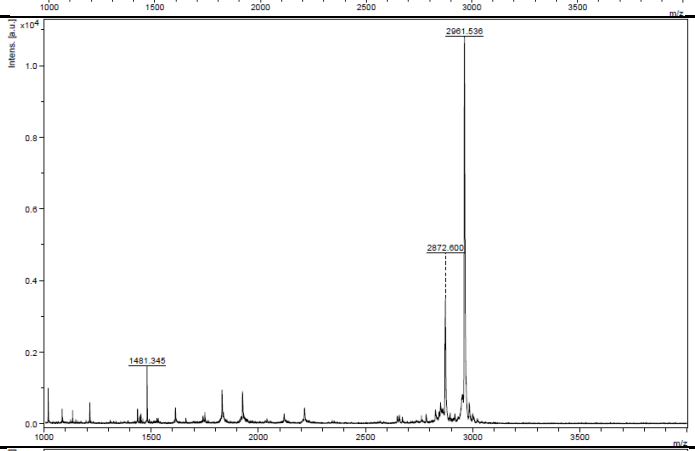
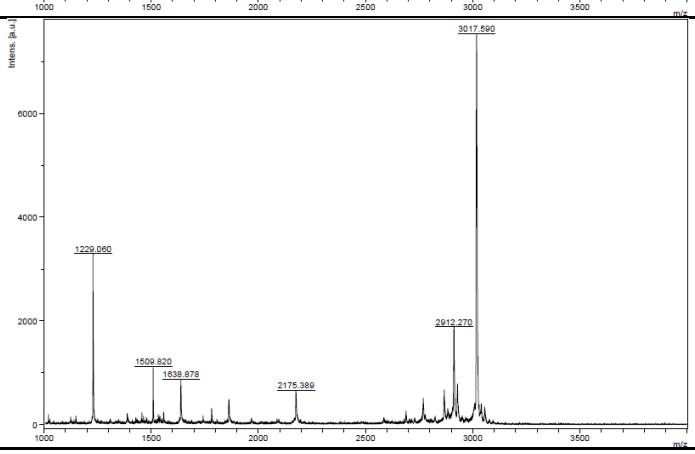
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.9
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.0
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2963.8
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.9

CPG-oligonucleotide + 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone T

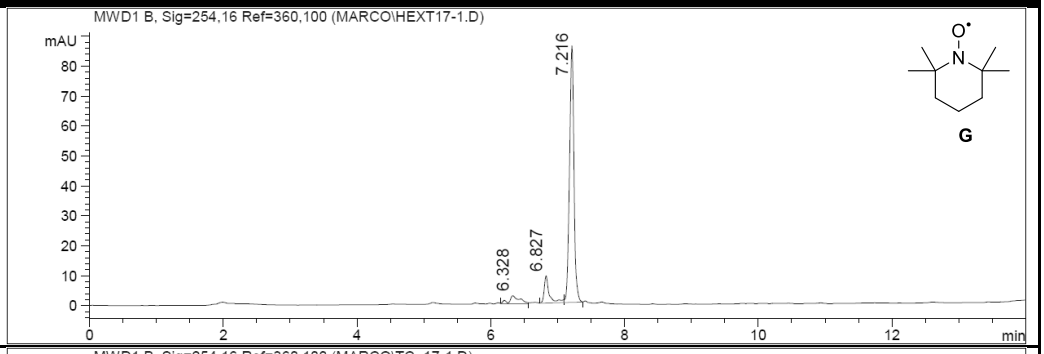
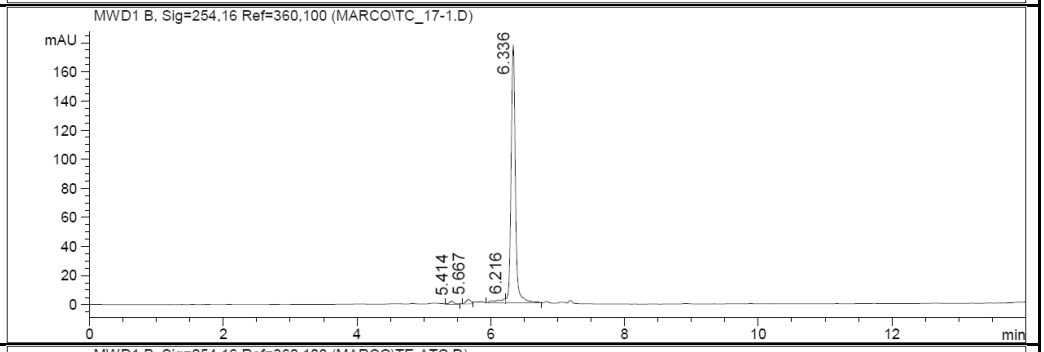
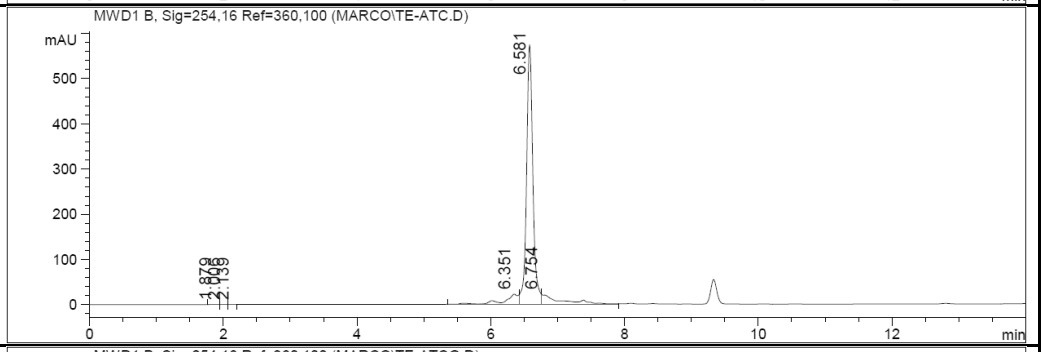
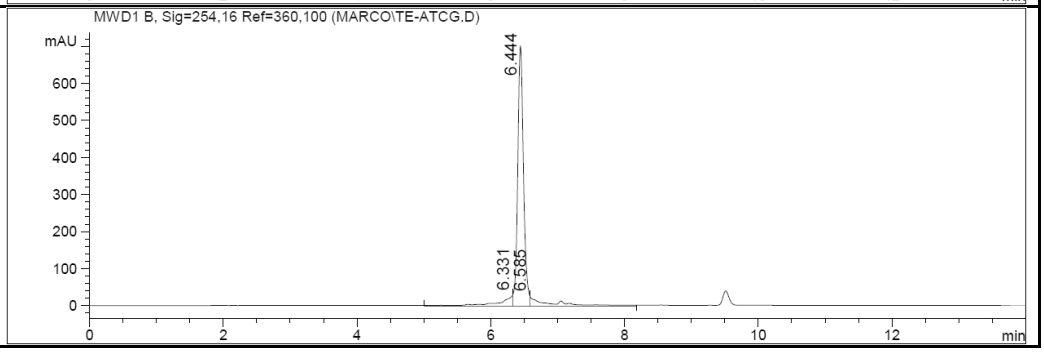
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone **T** (200 equiv., 4 µmol) in dry EtOH.

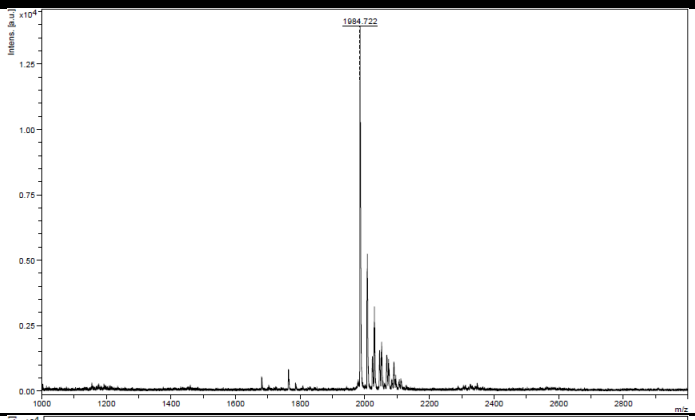
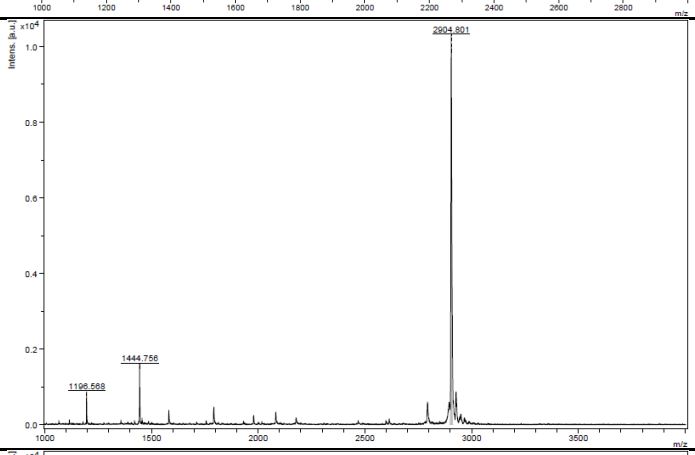
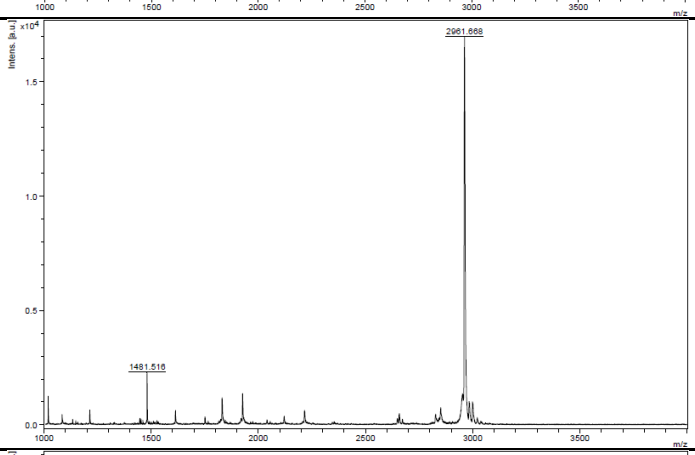
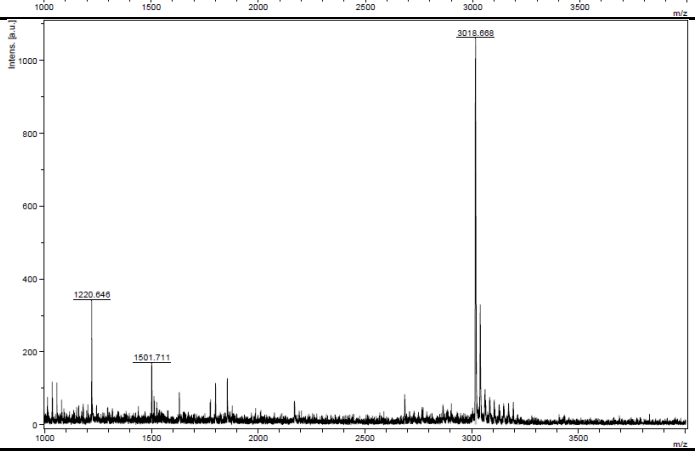
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.0
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2906.4
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.5
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3017.6

CPG-oligonucleotide + (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl G

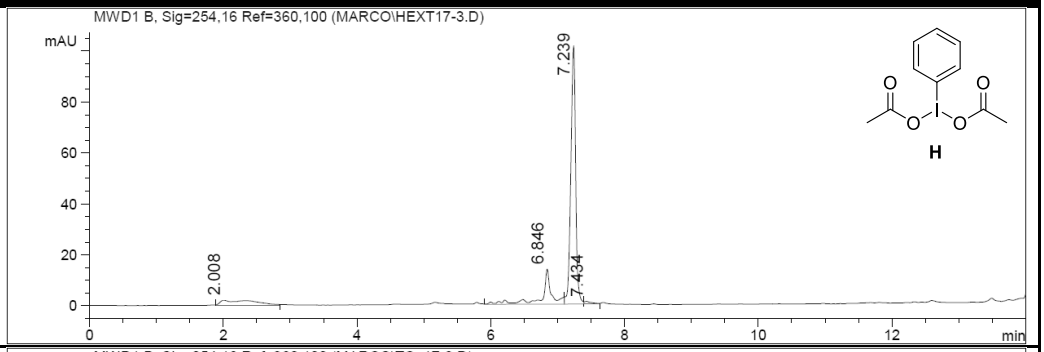
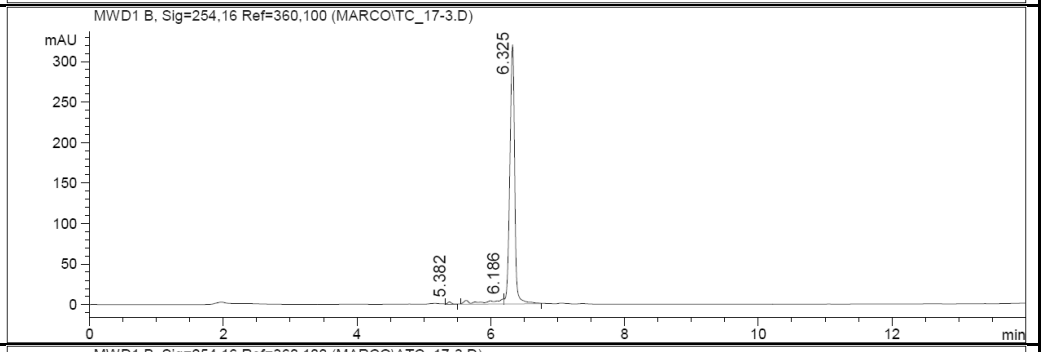
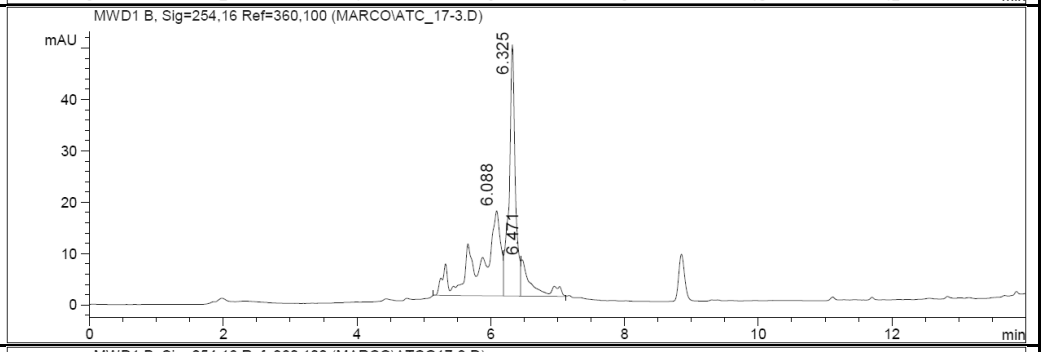
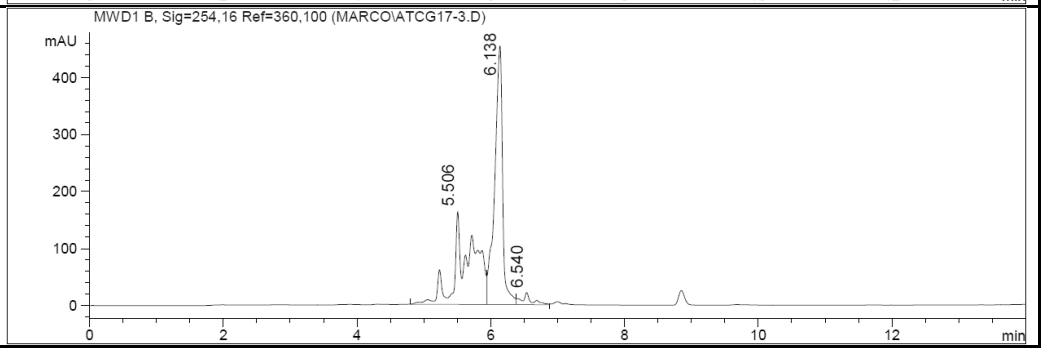
According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl **G** (200 equiv., 4 µmol) in dry ACN.

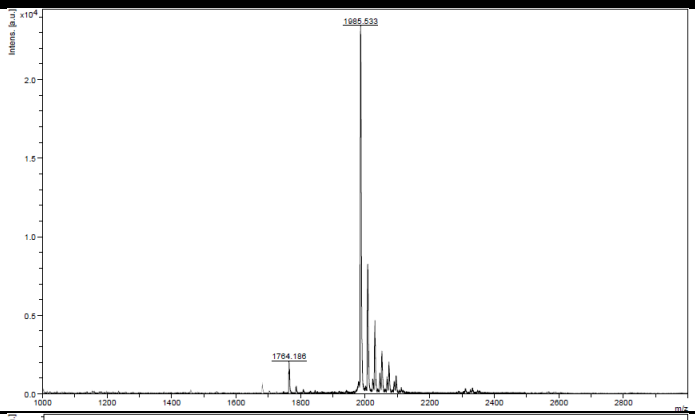
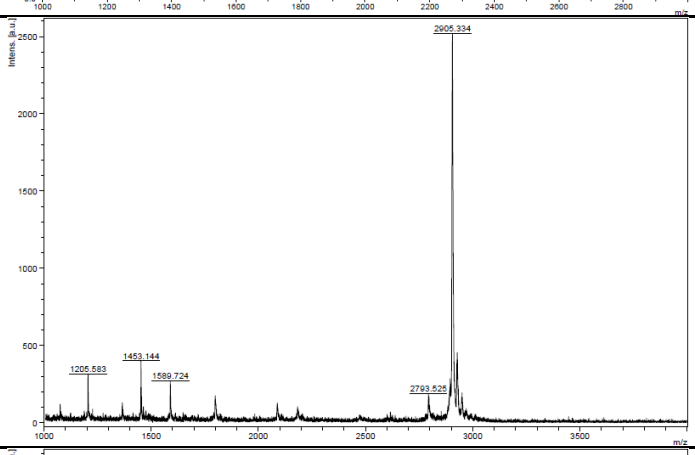
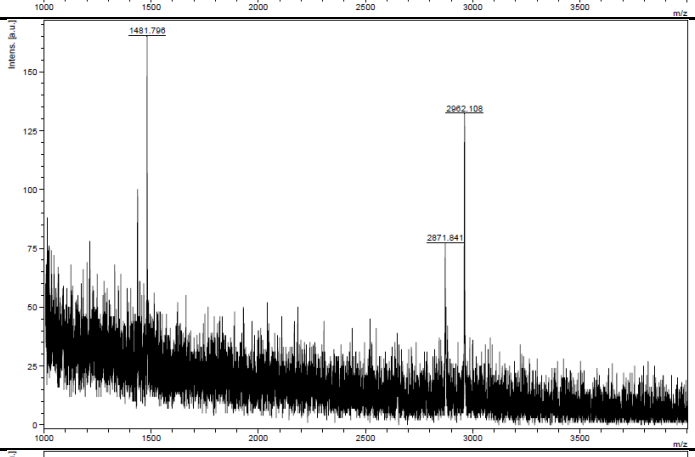
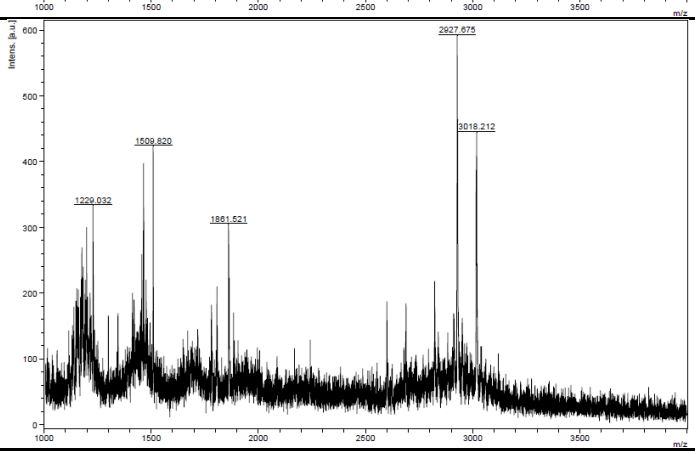
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1984.7
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2904.8
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2961.7
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.7

CPG-oligonucleotide + (Diacetoxyiodo)benzene H

According to the representative procedure (RP-04) solid support coupled oligonucleotide (20 nmol) was treated with (Diacetoxyiodo)benzene **H** (200 equiv., 4 µmol) in dry ACN.

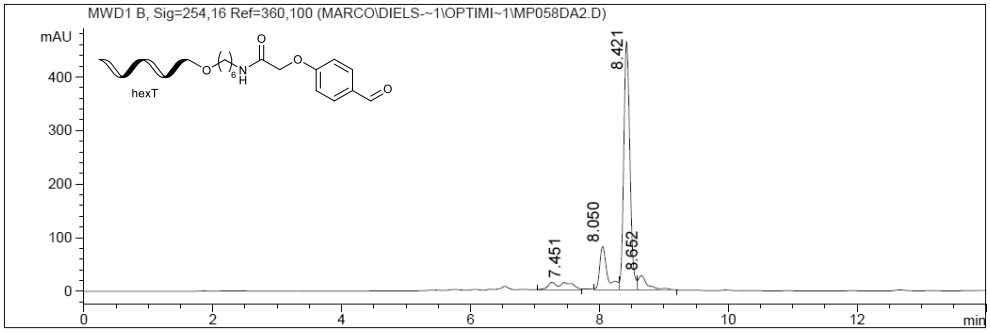
CPG-oligonucleotide	Analytical RP-HPLC-trace
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**	
10mer TC **5'-TTC CTC TCC T-3'-**	
10mer ATC **5'-TTA CTA CCT A-3'**	
10mer ATGC **5'-GTC ATG ATC T-3'**	

CPG-oligonucleotide	MALDI-MS spectra	
hexT-Ac **AcNH-$(CH_2)_6$-** **5'-TTT TTT-3'**		mass calc. = 1985.4 mass found = 1985.5
10mer TC **5'-TTC CTC TCC T-3'**		mass calc. = 2904.9 mass found =2905.3
10mer ATC **5'-TTA CTA CCT A-3'**		mass calc. = 2962.0 mass found = 2962.1
10mer ATGC **5'-GTC ATG ATC T-3'**		mass calc. = 3019.0 mass found = 3018.2

Synthesis of CPG-coupled oligonucleotide-aldehyde and -aniline conjugates

DNA conjugate 11: Following DMT removal, CPG-coupled hexT-C_6-NH_2 was reacted with 2-(4-formylphenoxy)acetic acid according to RP-06.

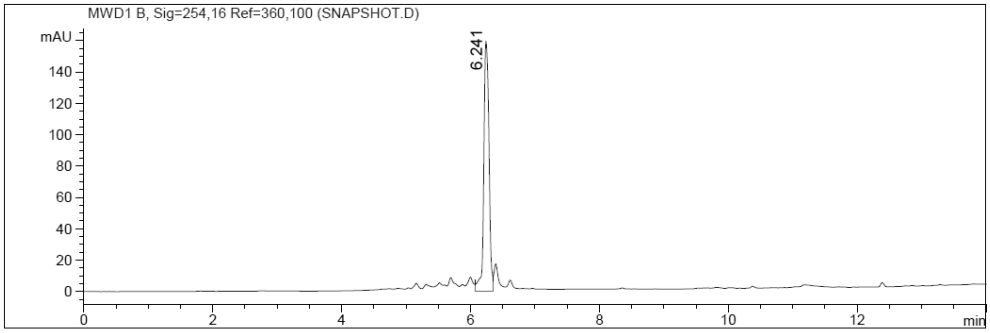
HPLC trace of crude reaction mixture 11 (Analytical RP-HPLC, Method-I)



Peak list:

Ret. Time	Width min	Height	Area	Area %
7.451	0.380	13.568	309.446	6.985
8.050	0.140	81.005	680.467	15.360
8.421	0.113	465.707	3157.925	71.284
8.652	0.172	27.277	282.228	6.371

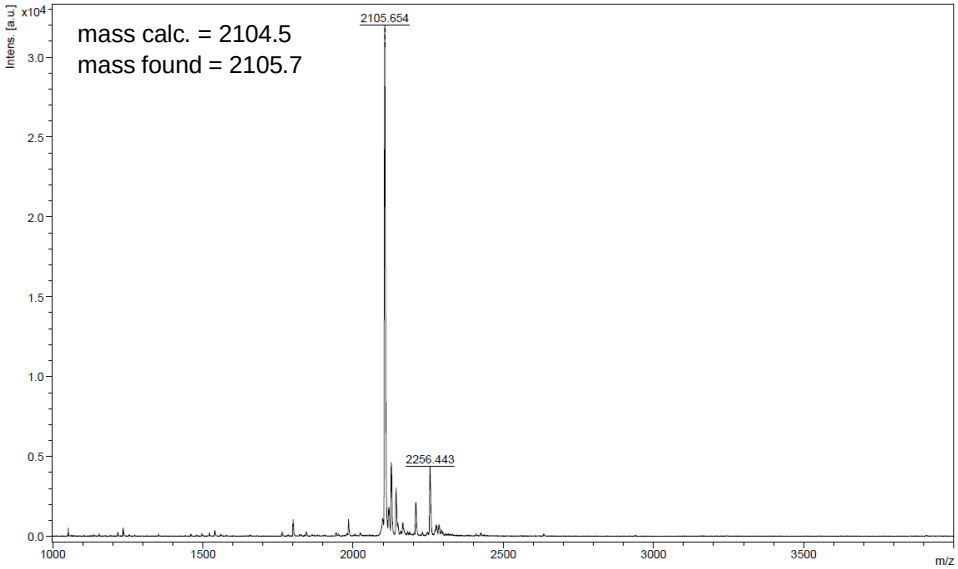
HPLC trace of crude reaction mixture 11 (Analytical RP-HPLC, Method-III)



Peak list:

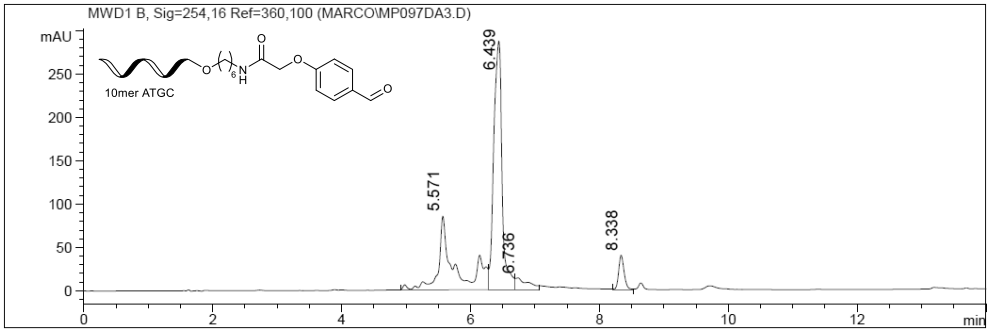
Ret. Time	Width min	Height	Area	Area %
6.241	0.089	159.216	887.480	100.000

MALDI-MS spectrum of crude reaction mixture 11



DNA conjugate 15a: Following DMT removal, CPG-coupled 10mer ATGC-C_6-NH_2 was reacted with 2-(4-formylphenoxy)acetic acid according to RP-06.

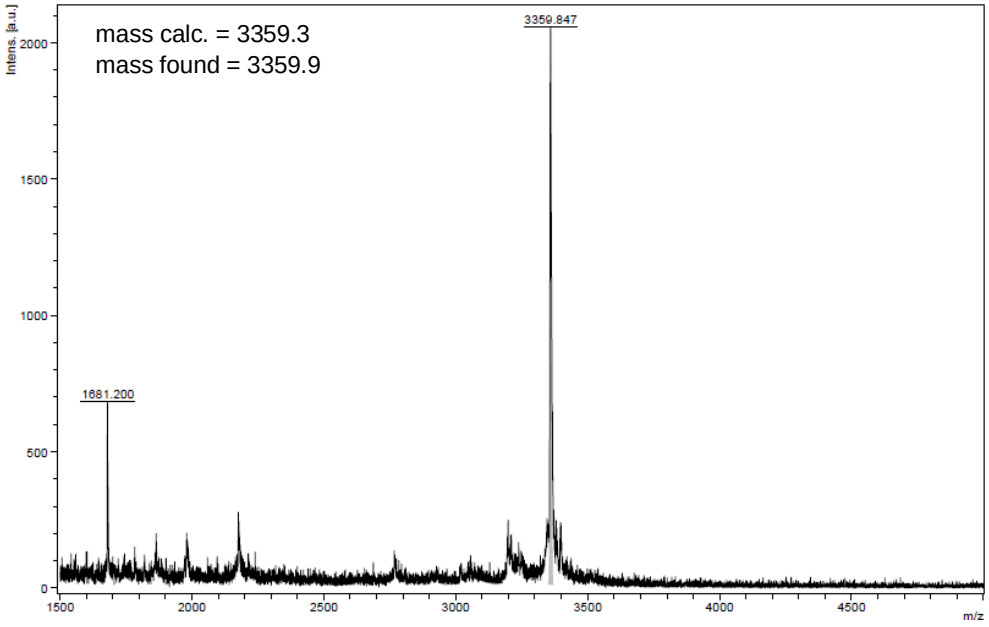
HPLC trace of crude reaction mixture 15a (Analytical RP-HPLC, Method-II)



Peak list:

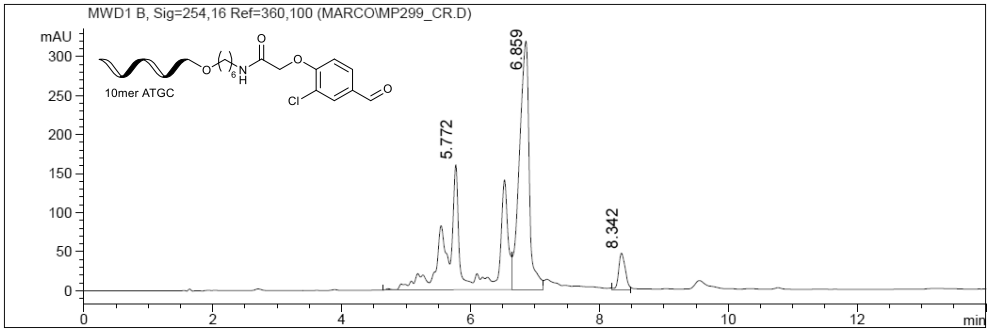
Ret. Time	Width min	Height	Area	Area %
5.571	0.289	85.209	1478.684	32.859
6.439	0.151	287.006	2591.899	57.597
6.736	0.244	13.652	199.884	4.442
8.338	0.096	39.738	229.610	5.102

MALDI-MS spectrum of crude reaction mixture 15a



DNA conjugate 15b: Following DMT removal, CPG-coupled 10mer ATGC-C_6-NH_2 was reacted with 2-(2-chloro-4-formylphenoxy)acetic acid according to RP-06.

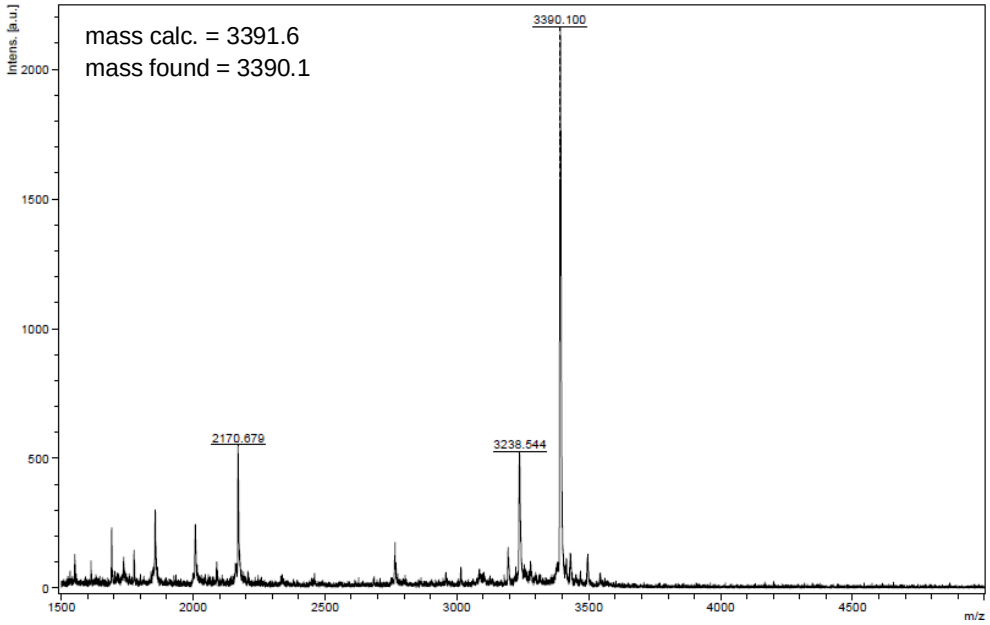
HPLC trace of crude reaction mixture 15b (Analytical RP-HPLC, Method-II)



Peak list:

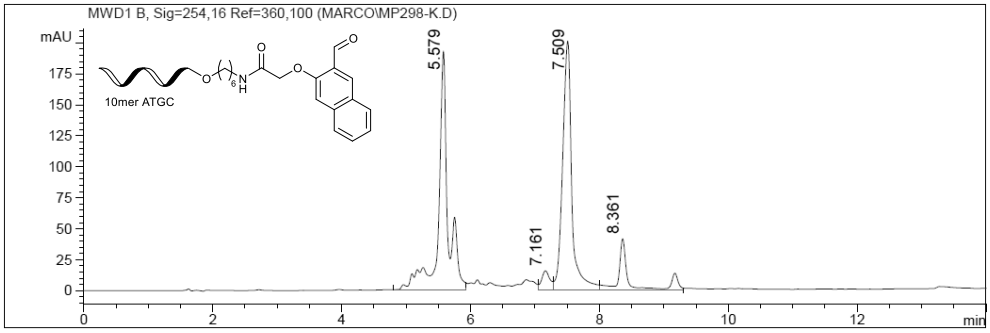
Ret. Time	Width min	Height	Area	Area %
5.772	0.363	160.782	3497.436	48.597
6.859	0.176	318.828	3368.118	46.800
8.342	0.119	46.536	331.252	4.603

MALDI-MS spectrum of crude reaction mixture 15b



DNA conjugate 15c: Following DMT removal, CPG-coupled 10mer ATGC-C_6-NH_2 was reacted with 2-((3-formylnaphthalen-2-yl)oxy)acetic acid according to RP-06.

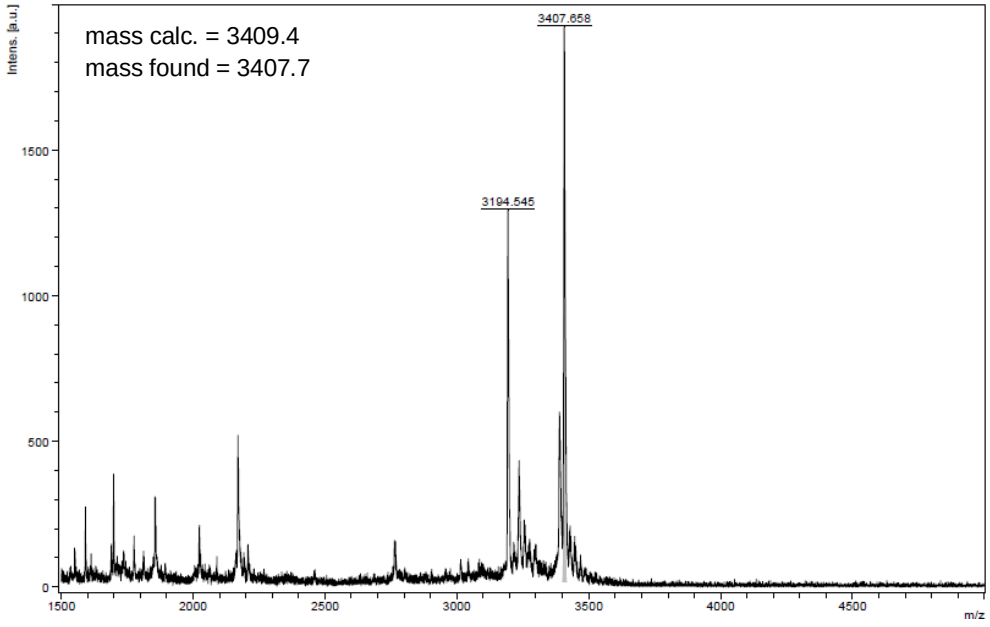
HPLC trace of crude reaction mixture 15c (Analytical RP-HPLC, Method-II)



Peak list:

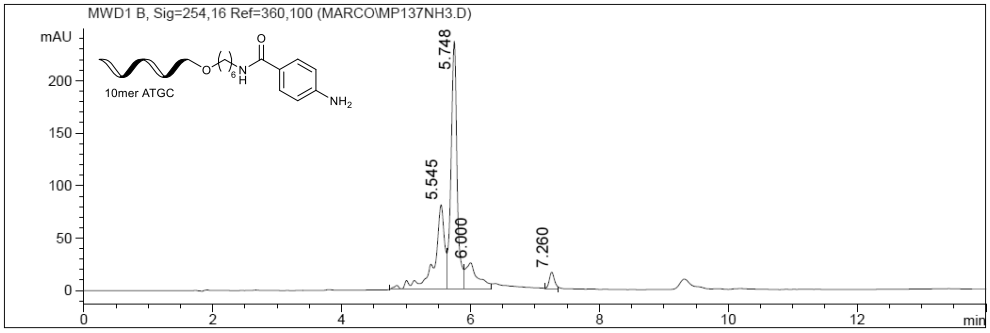
Ret. Time	Width min	Height	Area	Area %
5.579	0.169	192.695	1958.967	43.751
7.161	0.150	15.139	136.541	3.049
7.509	0.163	200.876	1960.796	43.792
8.361	0.171	41.176	421.236	9.408

MALDI-MS spectrum of crude reaction mixture 15c



DNA conjugate 17: Following DMT removal, CPG-coupled 10mer ATGC-C_6-NH_2 was reacted with Fmoc-4-aminobenzoic acid according to RP-06.

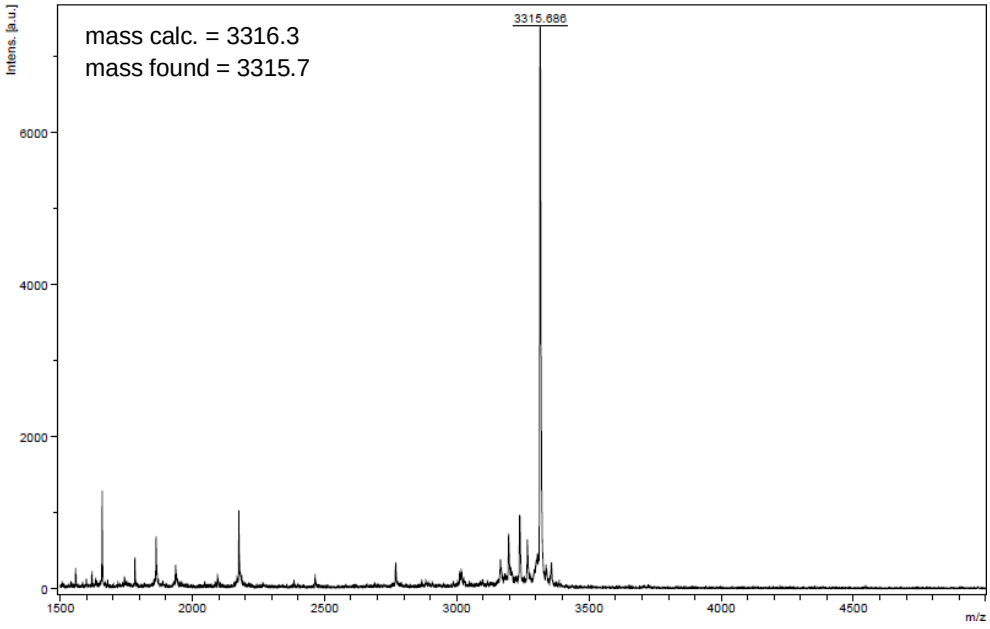
HPLC trace of crude reaction mixture 17 (Analytical RP-HPLC, Method-II)



Peak list:

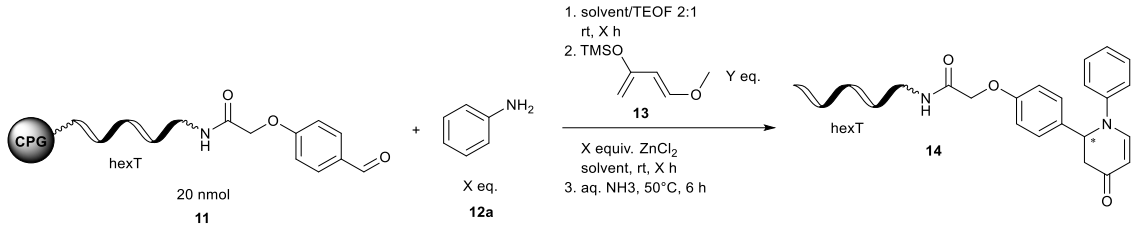
Ret. Time	Width min	Height	Area	Area %
5.545	0.185	80.235	889.637	31.150
5.748	0.108	236.329	1537.165	53.823
6.000	0.227	24.931	338.957	11.868
7.260	0.094	15.985	90.193	3.158

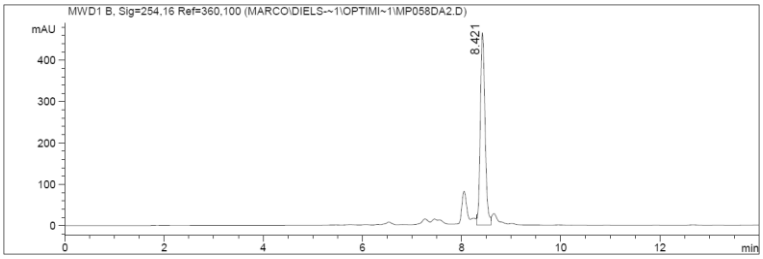
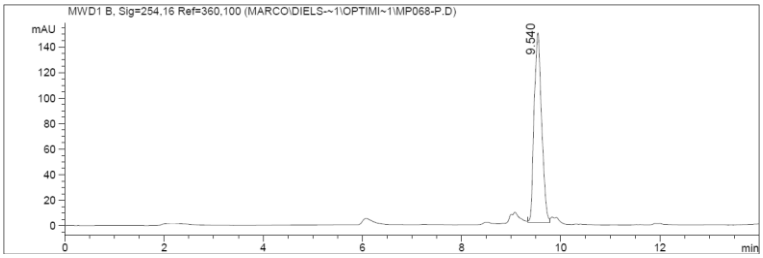
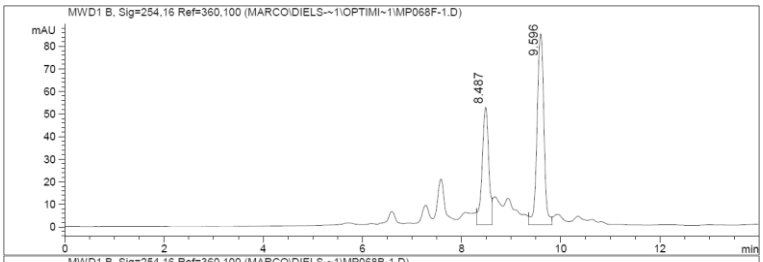
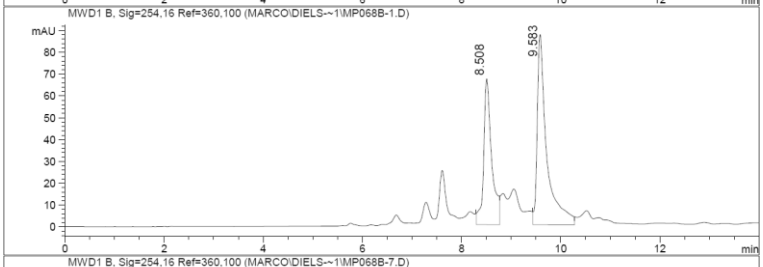
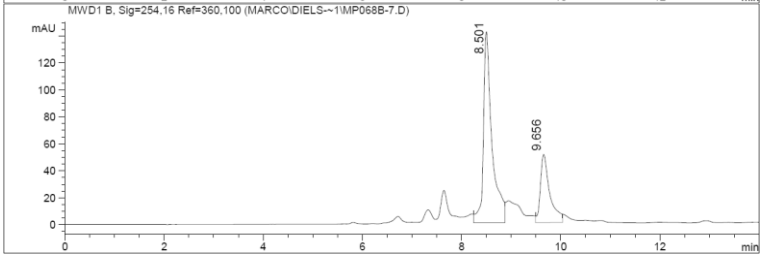
MALDI-MS spectrum of crude reaction mixture 17



ZnCl2-mediated aza-Diels-Alder reaction on CPG-coupled oligonucleotides

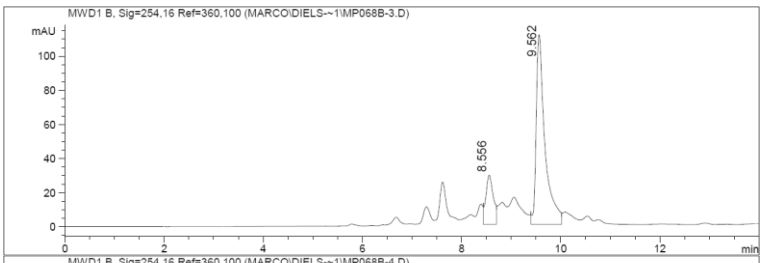
Table S5 Optimization of $ZnCl_2$-mediated aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled hexT-aldehyde conjugate.[a]



Entry	Reaction conditions[b]	HPLC trace of crude reaction mixture[c]
1	hexT-aldehyde conjugate **11**	
2	hexT-isoquinolone conjugate **14**	
3	1. 500 equiv. **12a** ***THF***/TEOF (2:1), 4 h, rt 2. 500 equiv. **13** 50 equiv. $ZnCl_2$ ***THF***, 1 h, rt => conversion 62 %	
4	1. 500 equiv. **12a** ***CH_2Cl_2***/TEOF (2:1), 4 h, rt 2. 500 equiv. **13** 50 equiv. $ZnCl_2$ ***CH_2Cl_2***, 1 h, rt => conversion 61 %	
5	1. 500 equiv. **12a** ***DCE***/TEOF (2:1), 4 h, rt 2. 500 equiv. **13** 50 equiv. $ZnCl_2$ ***DCE***, 1 h, rt => conversion 28 %	

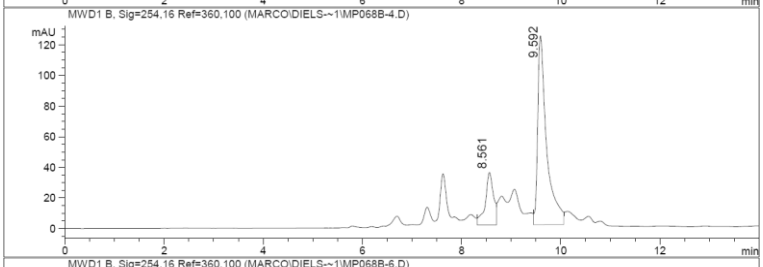
6 1. 500 equiv. **12a**
ACN/TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
50 equiv. $ZnCl_2$
ACN, 1 h, rt

=> conversion 82 %



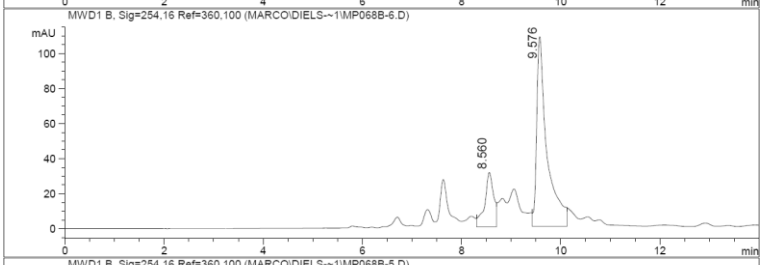
7 1. 500 equiv. **12a**
MeOH/TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
50 equiv. $ZnCl_2$
MeOH, 1 h, rt

=> conversion 80 %



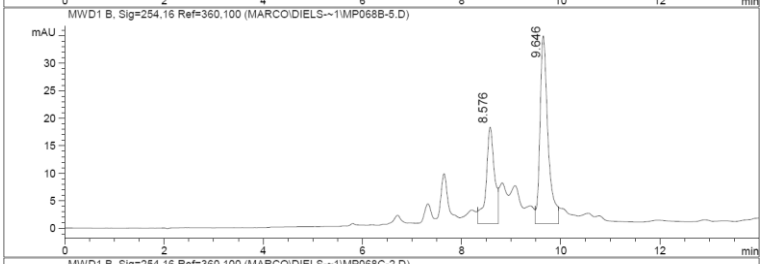
8 1. 500 equiv. **12a**
EtOH/TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
50 equiv. $ZnCl_2$
EtOH, 1 h, rt

=> conversion 80 %



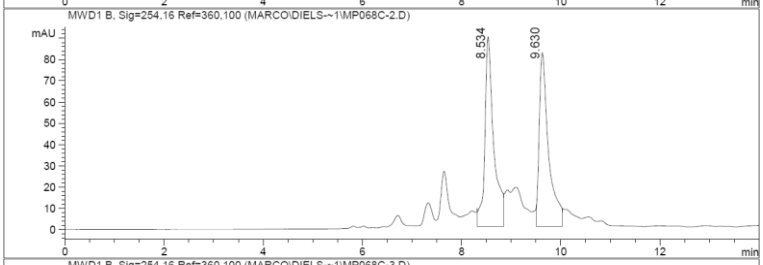
9 1. 500 equiv. **12a**
Toluene /TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
50 equiv. $ZnCl_2$
Toluene, 1 h, rt

=> conversion 65 %



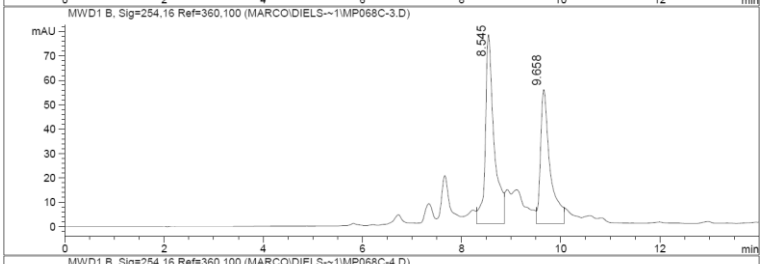
10 1. ***1000 equiv.*** **12a**
THF/TEOF (2:1), 4 h, rt
2. ***1000 equiv.*** **13**
50 equiv. $ZnCl_2$
THF, 1 h, rt

=> conversion 49 %



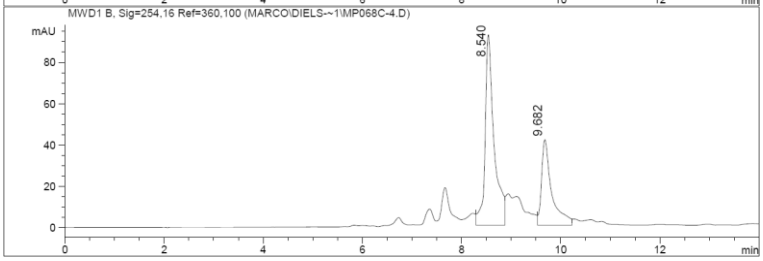
11 1. ***2000 equiv.*** **12a**
THF/TEOF (2:1), 4 h, rt
2. ***2000 equiv.*** **13**
50 equiv. $ZnCl_2$
THF, 1 h, rt

=> conversion 43 %



12 1. ***4000 equiv.*** **12a**
THF/TEOF (2:1), 4 h, rt
2. ***4000 equiv.*** **13**
50 equiv. $ZnCl_2$
THF, 1 h, rt

=> conversion 34 %



13

1. ***4000 equiv.* 12a**
   THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
   50 equiv. $ZnCl_2$
   THF, 1 h, rt

   => conversion 33 %

14

1. 500 equiv. **12a**
   THF/TEOF (2:1), 4 h, rt
2. ***4000 equiv.* 13**
   50 equiv. $ZnCl_2$
   THF, 1 h, rt

   => conversion 73 %

15

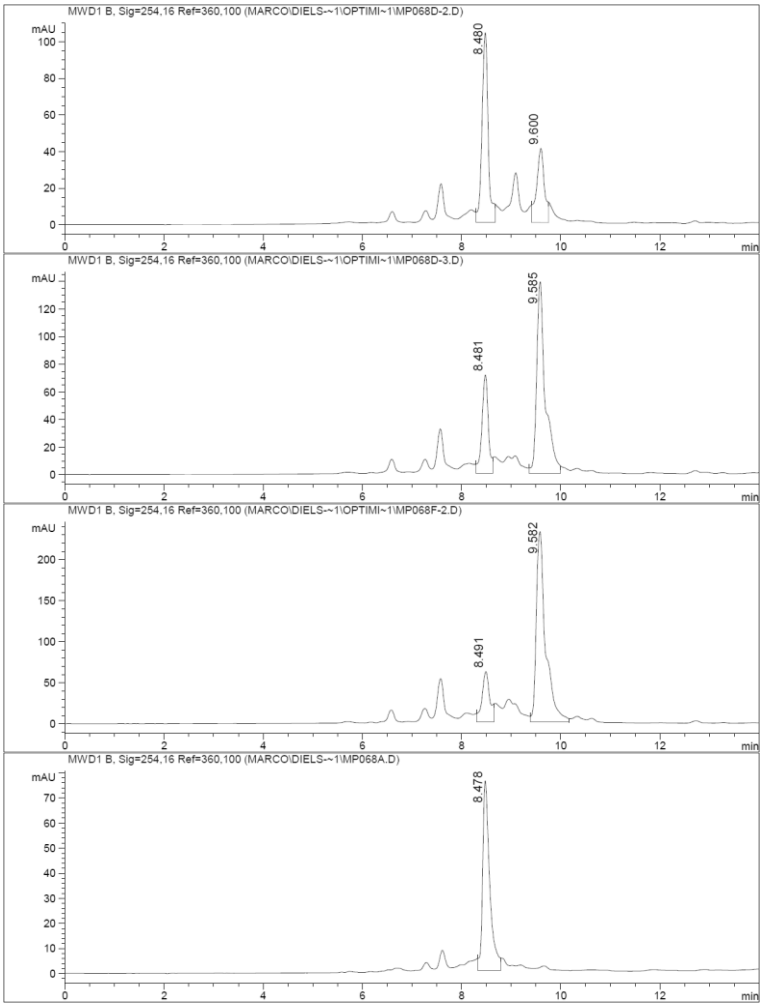
1. 500 equiv. **12a**
   THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
   100 equiv. $ZnCl_2$
   THF, 1 h, rt

   => conversion 82%

16

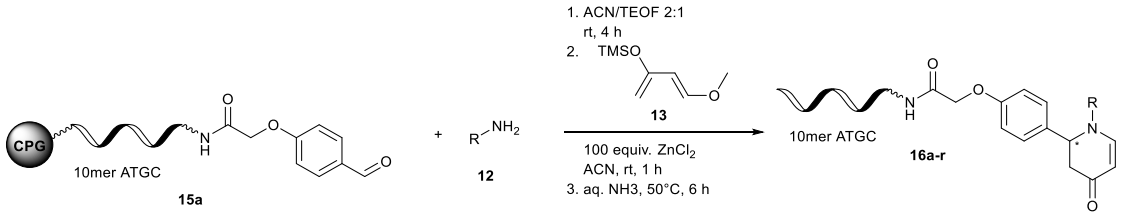
1. 500 equiv. **12a**
   THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **13**
   THF, 1 h, rt

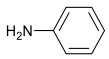
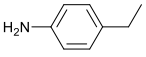
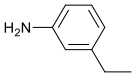
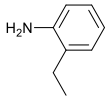
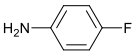
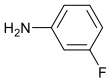
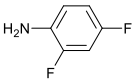
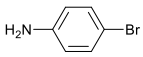
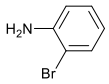
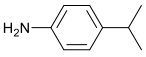
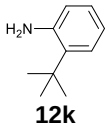
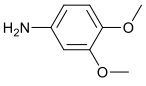
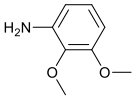
   => conversion < 5%

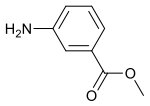
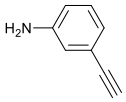
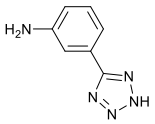
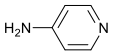


[a] Condensation of CPG-coupled hexT aldehyde conjugate **11** (20 nmol) with aniline **12a** (X equiv.) in 36 µL of indicated solvent/triethyl orthoformate (2:1) at ambient temperature for 4 h, then $ZnCl_2$ (X equiv.) suspended in 30 µL of indicated solvent and Danishefsky's diene **13** (X equiv.) were added, the reaction mixture was shaken at ambient temperature for 1 h. [b] Changed parameters are in bold and italic. [c] Analytical RP-HPLC, Method-I. TEOF = triethyl orthoformate.

Table S6 – Scope of $ZnCl_2$-mediated aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled 10mer ATGC oligonucleotide-aldehyde conjugate using different amines.[a]



Entry	Product	Amine	Conversion [%][b]	$Mass_{calc.}$ $Mass_{found}$[c]
1	**16a**	 **12a**	80	3502.5 3503.0
2	**16b**	 **12b**	83	3530.6 3530.6
3	**16c**	 **12c**	78	3530.6 3530.7
4	**16d**	 **12d**	21	3530.6 3530.5
5	**16e**	 **12e**	82	3520.5 3522.4
6	**16f**	 **12f**	75	3520.5 3518.2
7	**16g**	 **12g**	63	3538.5 3540.5
8	**16h**	 **12h**	75	3581.4 3582.0
9	**16i**	 **12i**	< 5	3581.4 n.d.
10	**16j**	 **12j**	80	3544.6 3545.1
11	**16k**	 **12k**	< 5	3558.6 n.d.
12	**16l**	 **12l**	71	3562.6 3564.0
13	**16m**	 **12m**	27	3562.6 3563.8

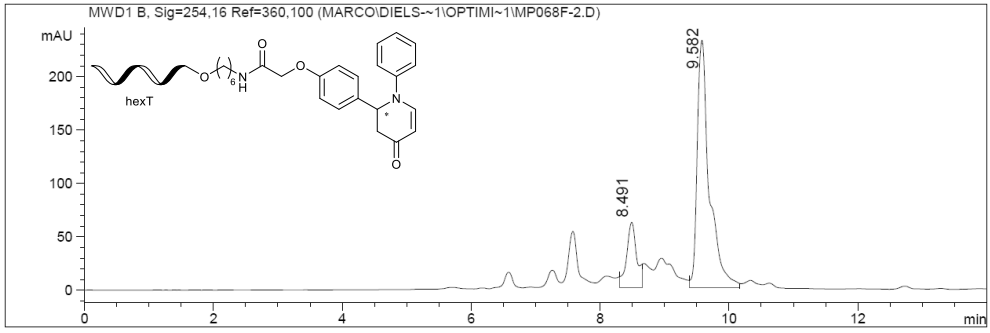
14	**16n**	 **12n**	64	3560.5 n.d. cleaved ester 3546.5 3545.4
15	**16o**	 **12o**	70	3526.5 3527.2
16[d]	**16p**	 **12p**	63	3570.6 3570.6
17[d]	**16q**	 **12q**	< 5	3503.5 n.d.
18[e,f,g]	**16r**	 **12r**	56	3468.5 3469.1

[a] Condensation of CPG-coupled oligonucleotide conjugate **13** (20 nmol) with amine **14** (500 equiv., 10 µmol) in 36 µL acetonitrile/triethyl orthoformate (2:1) at ambient temperature for 4 h, then addition of $ZnCl_2$ (100 equiv., 2 µmol) dissolved in 30 µL acetonitrile and Danishefsky's diene **15** (1000 equiv., 20 µmol) at ambient temperature for 1 h. DNA cleavage with 30 % aqueous ammonia at 50 °C for 6 h. [b] Determined by analytical RP-HPLC analysis. [c] Measured by MALDI-MS. [d] Dimethyl sulfoxid was used instead of acetonitrile. [e] 1000 equiv. of amine were used. [d] $Yb(OTf)_3$ was used instead of $ZnCl_2$. [g] 2nd step of the reaction was performed overnight at 35 °C . 10mer ATGC = 5'-GTC ATG ATC T-3'. n.d. = not detected.

Products of aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled 10mer ATGC oligonucleotide-aldehyde conjugate

DNA conjugate 14: CPG-coupled hexT-aldehyde conjugate **11** was reacted with aniline **12a** and Danishefsky's diene **13** according to RP-07.

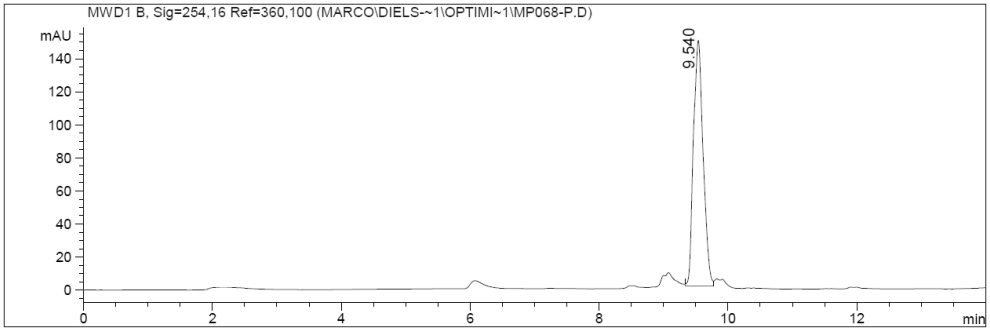
HPLC trace of crude reaction mixture 14 (Analytical RP-HPLC, Method-I)



Peak list:

Ret. Time	Width min	Height	Area	Area %
8.491	0.183	61.121	672.861	18.256
9.582	0.217	231.477	3012.743	81.744

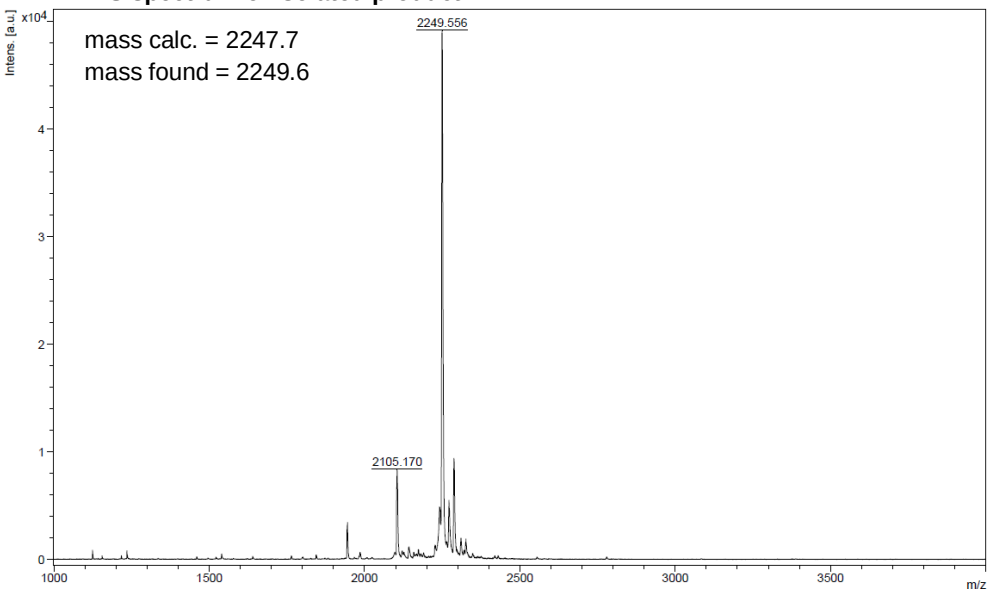
HPLC trace of isolated product 14 (Analytical RP-HPLC, Method-I)



Peak list:

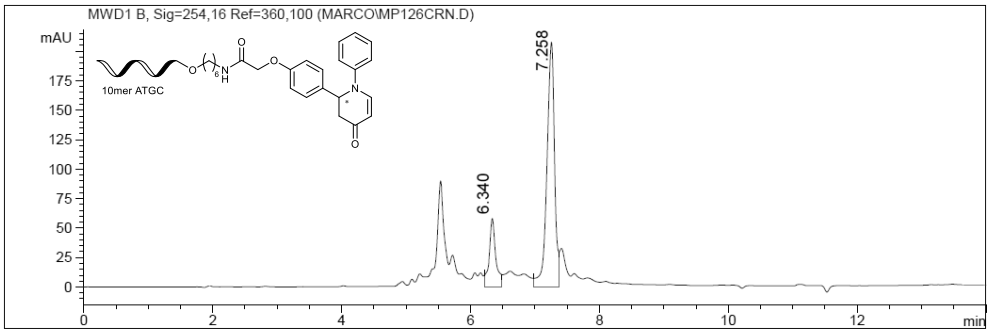
Ret. Time	Width min	Height	Area	Area %
9.540	0.174	148.892	1551.445	100.000

MALDI-MS spectrum of isolated product 14



DNA conjugate 16a: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with aniline **12a** and Danishefsky's diene **13** according to RP-07.

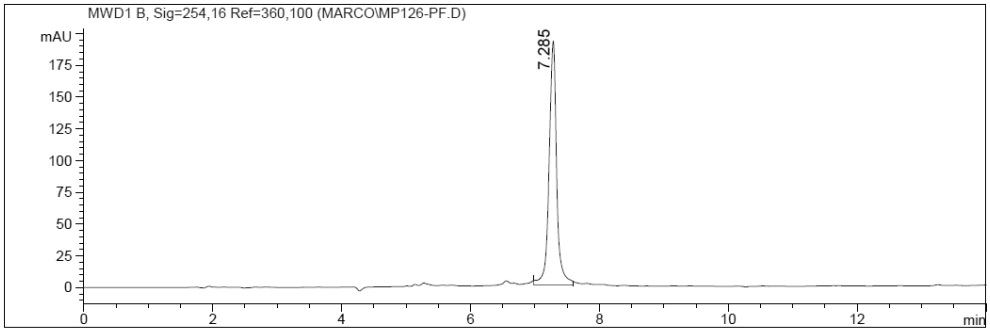
HPLC trace of crude reaction mixture 16a (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.340	0.119	58.214	417.263	19.674
7.258	0.136	208.242	1703.613	80.326

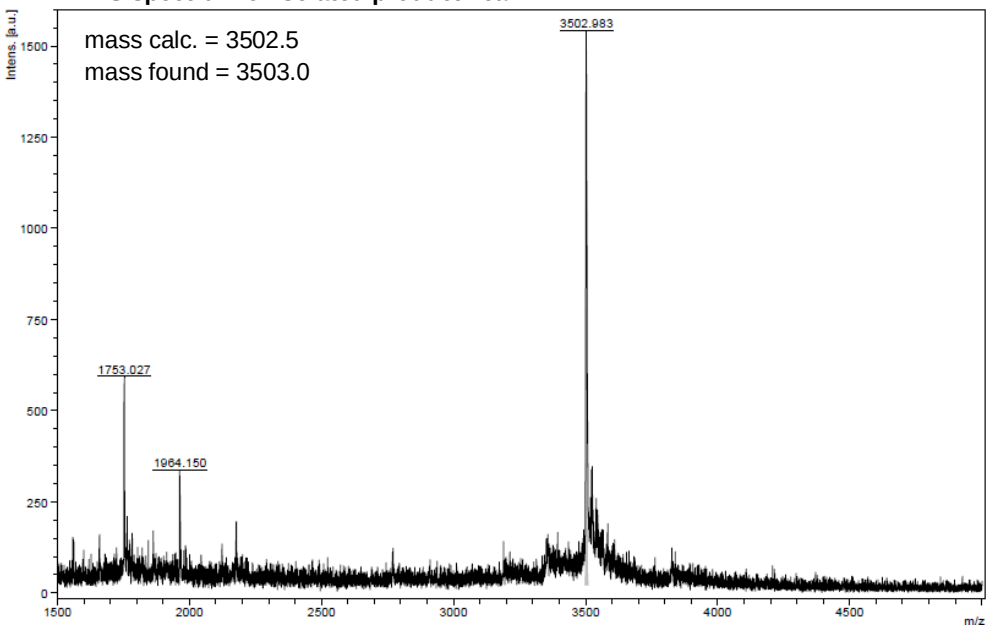
HPLC trace of isolated product 16a (Analytical RP-HPLC, Method-II)



Peak list:

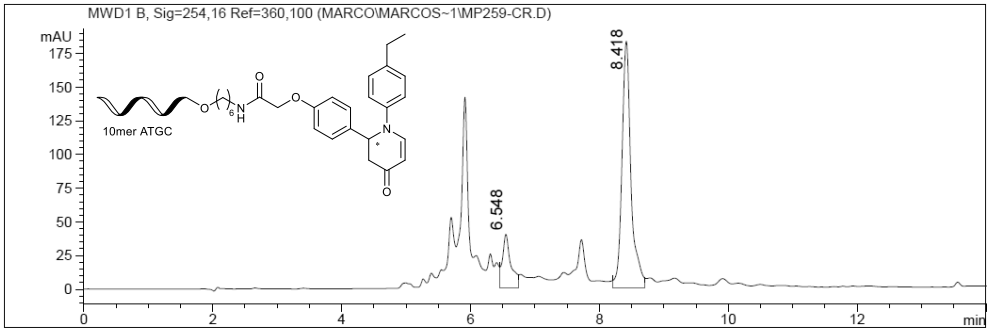
Ret. Time	Width min	Height	Area	Area %
7.285	0.137	192.411	1581.263	100.000

MALDI-MS spectrum of isolated product 16a



DNA conjugate 16b: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-ethylaniline **12b** and Danishefsky's diene **13** according to RP-07.

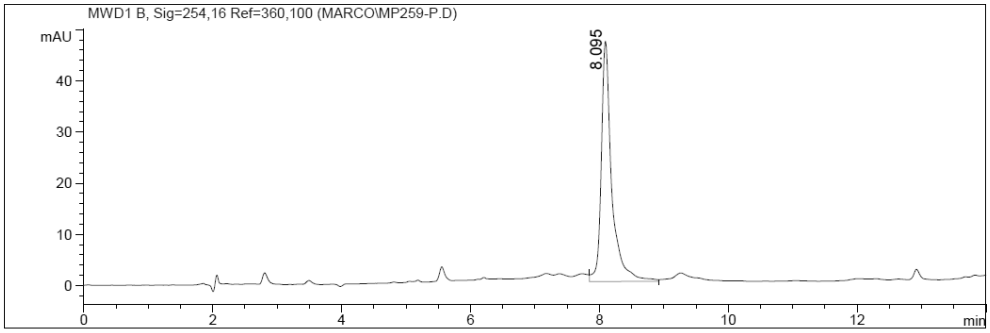
HPLC trace of crude reaction mixture 16b (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.548	0.152	40.113	366.884	17.142
8.418	0.161	183.156	1773.384	82.858

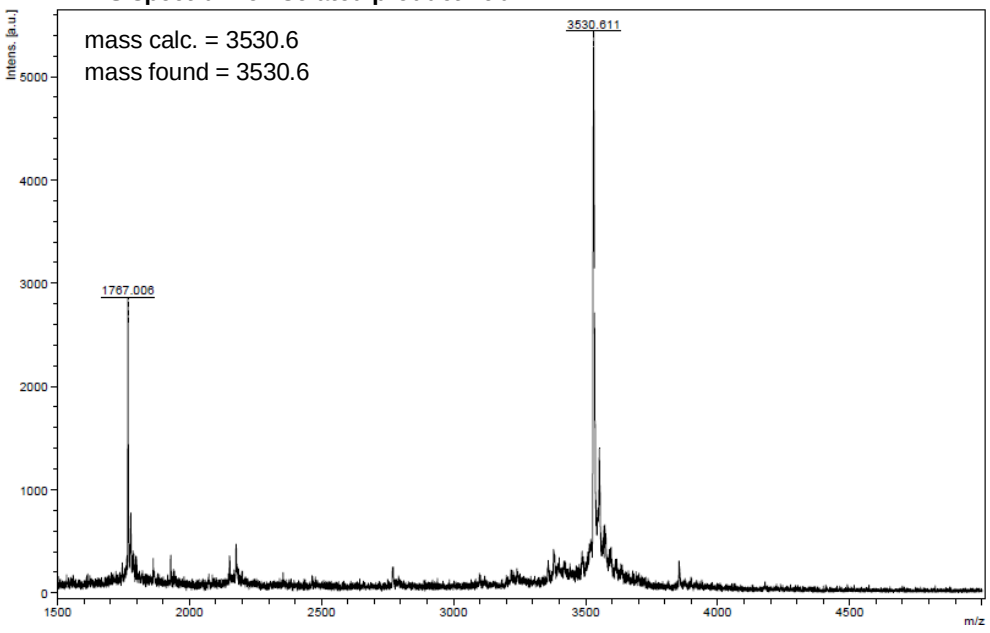
HPLC trace of isolated product 16b (Analytical RP-HPLC, Method-II)



Peak list:

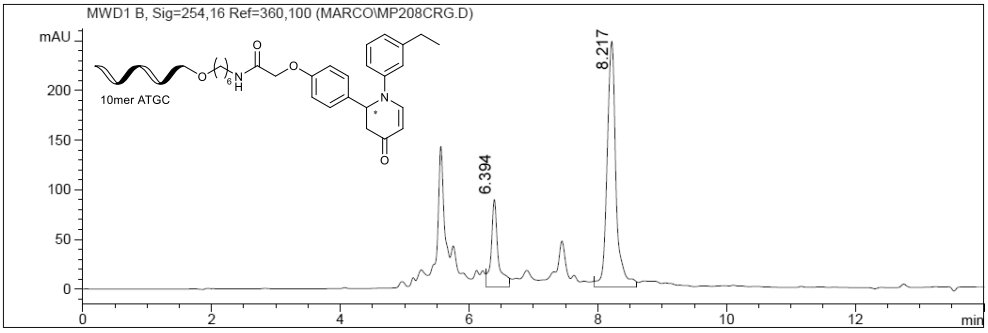
Ret. Time	Width min	Height	Area	Area %
8.095	0.163	46.939	527.236	100.000

MALDI-MS spectrum of isolated product 16b



DNA conjugate 16c: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-ethylaniline **12c** and Danishefsky's diene **13** according to RP-07.

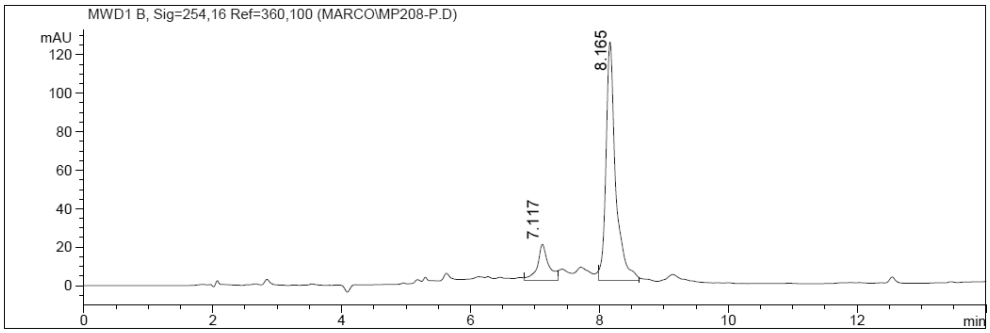
HPLC trace of crude reaction mixture 16c (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.394	0.126	88.915	671.706	22.094
8.217	0.159	247.953	2368.533	77.906

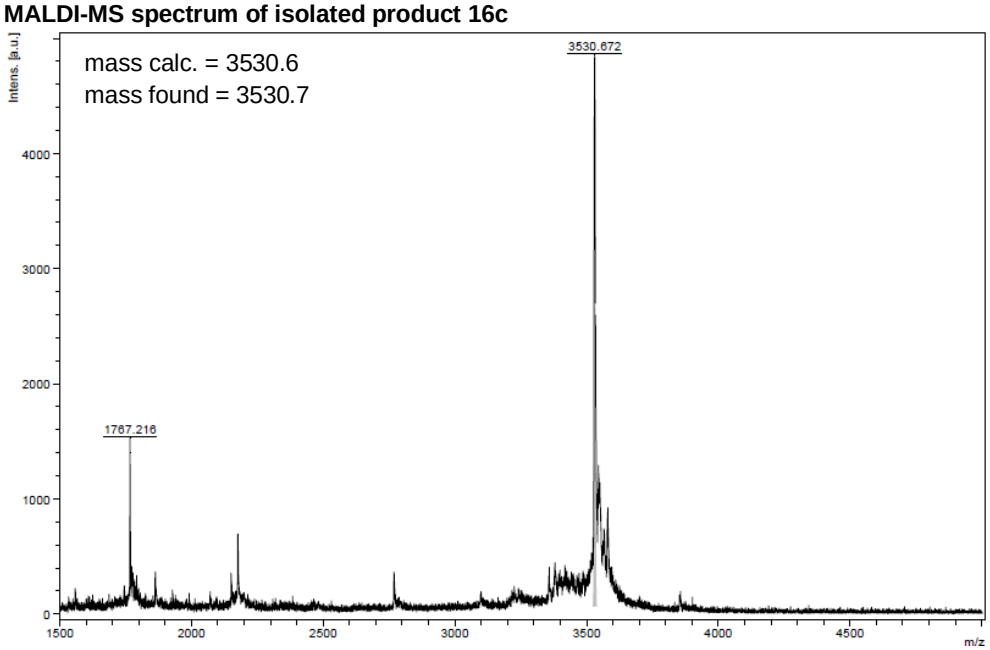
HPLC trace of isolated product 16c (Analytical RP-HPLC, Method-II)



Peak list:

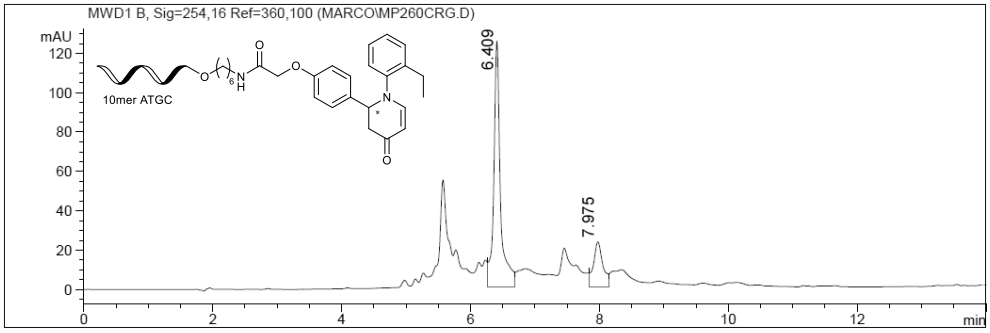
Ret. Time	Width min	Height	Area	Area %
7.117	0.200	18.678	223.737	14.897
8.165	0.172	123.940	1278.181	85.103

MALDI-MS spectrum of isolated product 16c



DNA conjugate 16d: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-ethylaniline **12d** and Danishefsky's diene **13** according to RP-07.

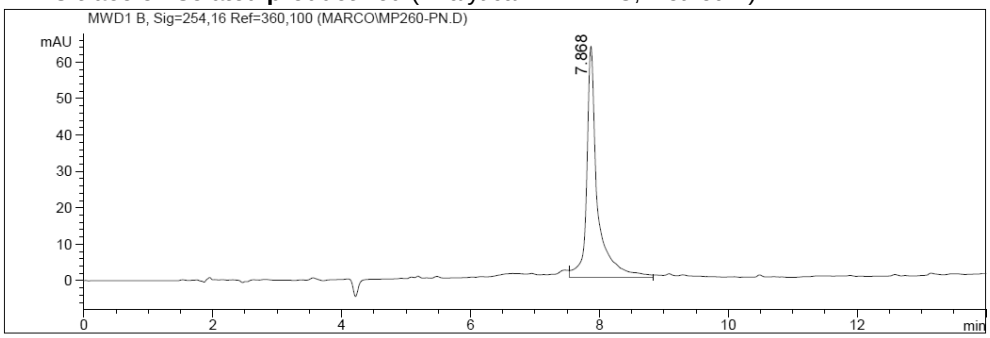
HPLC trace of crude reaction mixture 16d (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.409	0.118	125.205	888.869	79.180
7.975	0.170	22.931	233.718	20.820

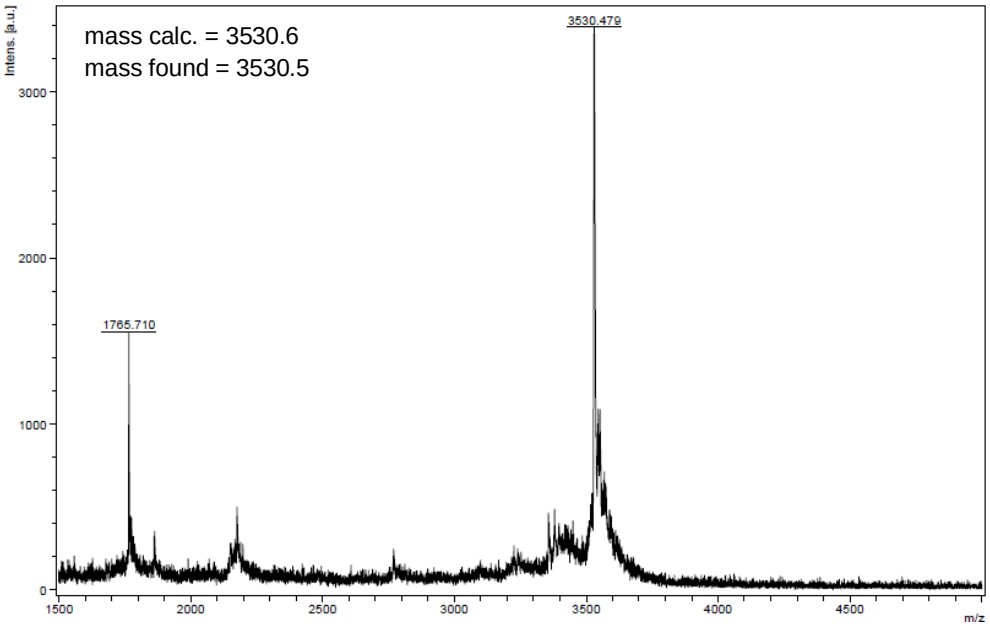
HPLC trace of isolated product 16d (Analytical RP-HPLC, Method-II)



Peak list:

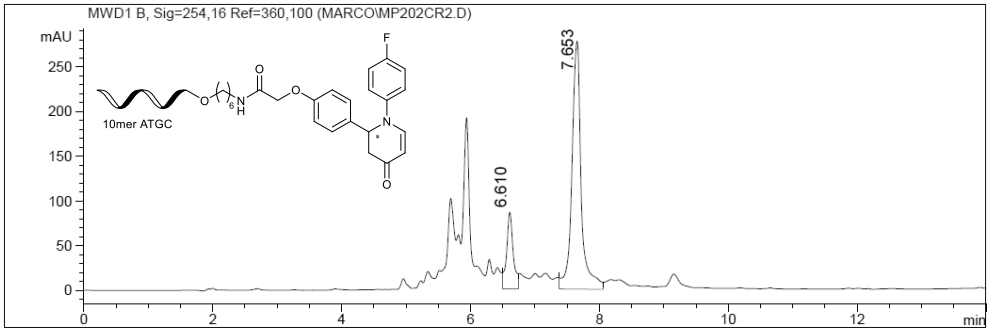
Ret. Time	Width min	Height	Area	Area %
7.868	0.163	63.501	734.635	100.000

MALDI-MS spectrum of isolated product 16d



DNA conjugate 16e: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-fluoroaniline **12e** and Danishefsky's diene **13** according to RP-07.

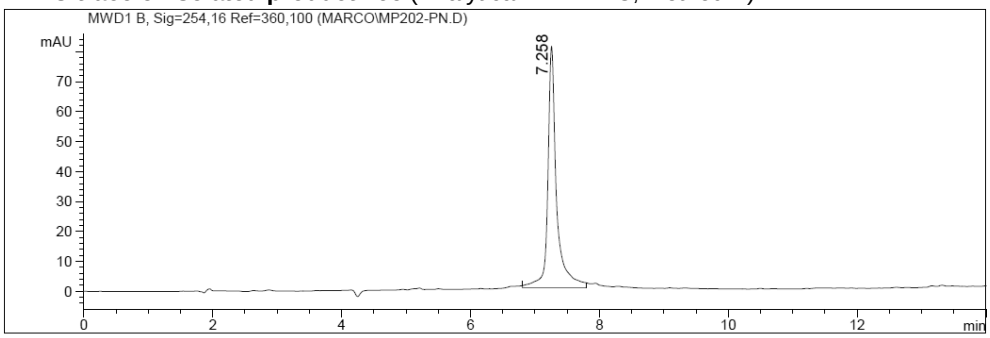
HPLC trace of crude reaction mixture 16e (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.610	0.119	85.910	615.488	17.943
7.653	0.169	277.660	2814.702	82.057

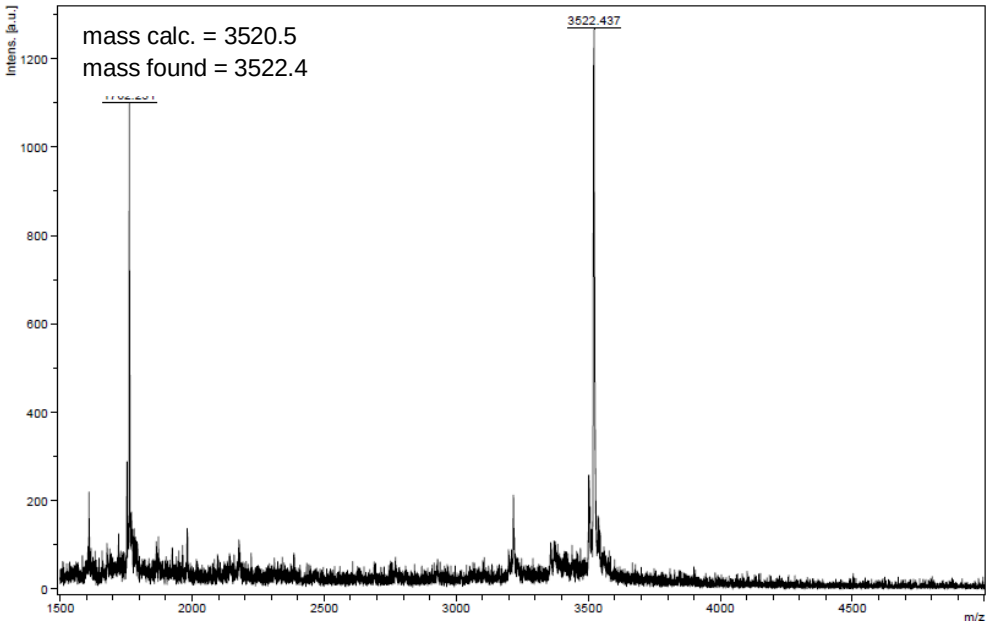
HPLC trace of isolated product 16e (Analytical RP-HPLC, Method-II)



Peak list:

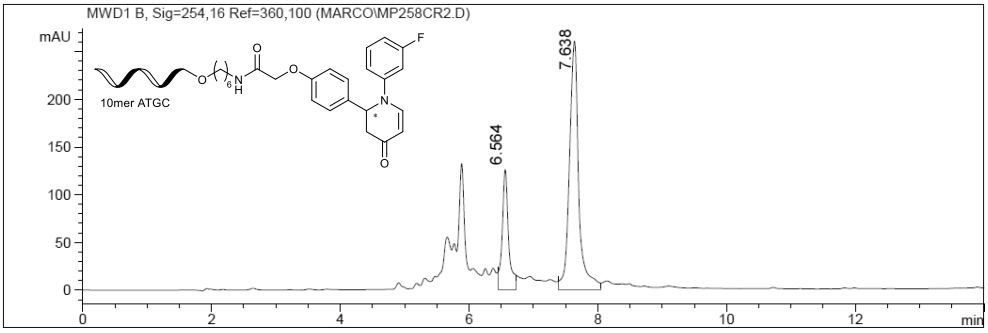
Ret. Time	Width min	Height	Area	Area %
7.258	0.157	80.713	759.141	100.000

MALDI-MS spectrum of isolated product 16e



DNA conjugate 16f: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-fluoroaniline **12f** and Danishefsky's diene **13** according to RP-07.

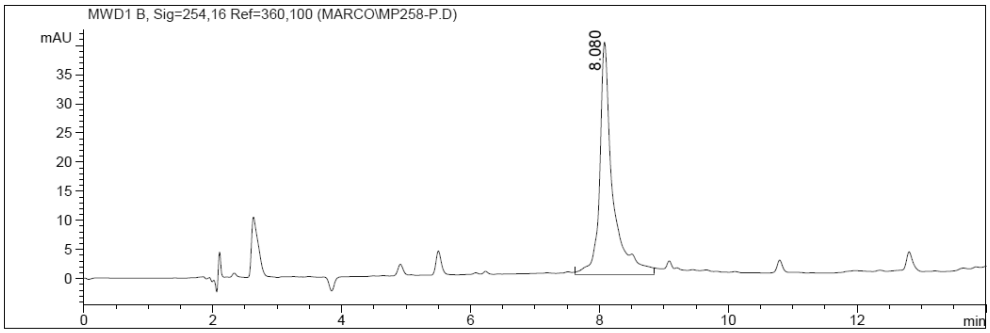
HPLC trace of crude reaction mixture 16f (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.564	0.115	126.466	869.415	24.985
7.638	0.167	260.806	2610.369	75.015

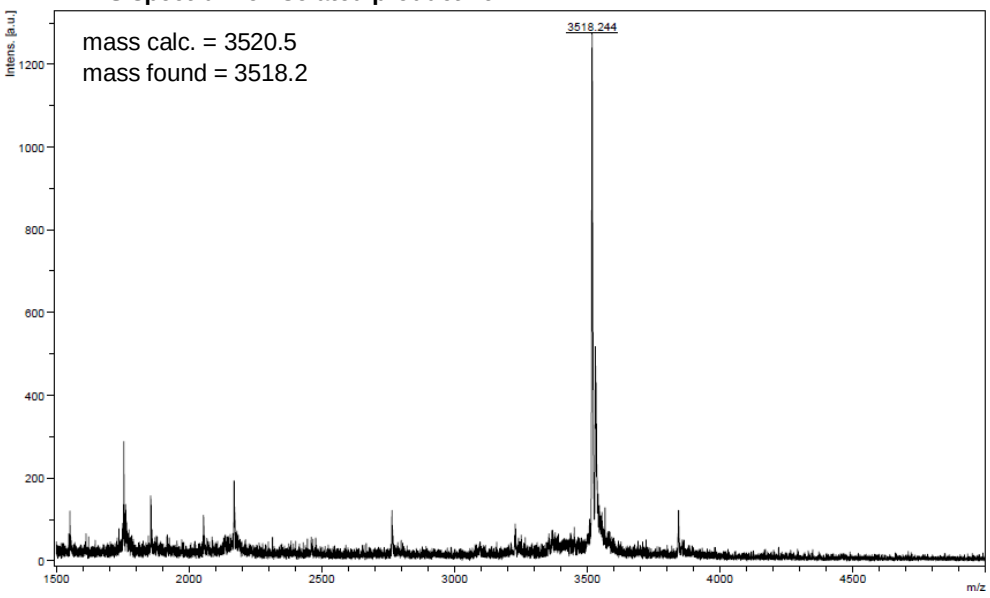
HPLC trace of isolated product 16f (Analytical RP-HPLC, Method-II)



Peak list:

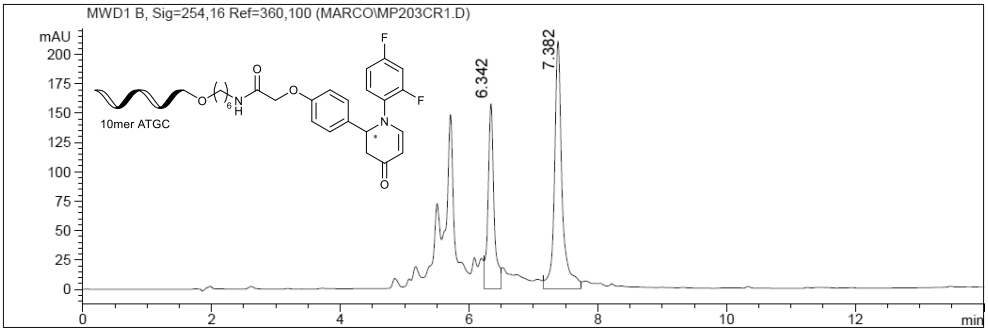
Ret. Time	Width min	Height	Area	Area %
8.080	0.233	39.982	559.062	100.000

MALDI-MS spectrum of isolated product 16f



DNA conjugate 16g: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2,4-difluoroaniline **12g** and Danishefsky's diene **13** according to RP-07.

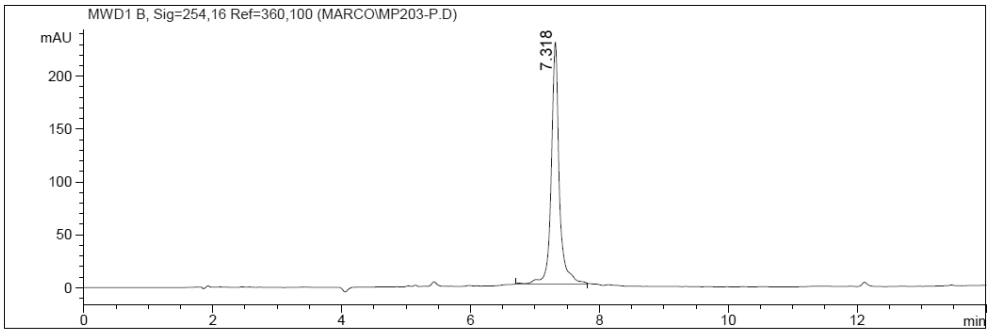
HPLC trace of crude reaction mixture 16g (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.342	0.106	158.038	1001.661	36.776
7.382	0.136	211.071	1722.049	63.224

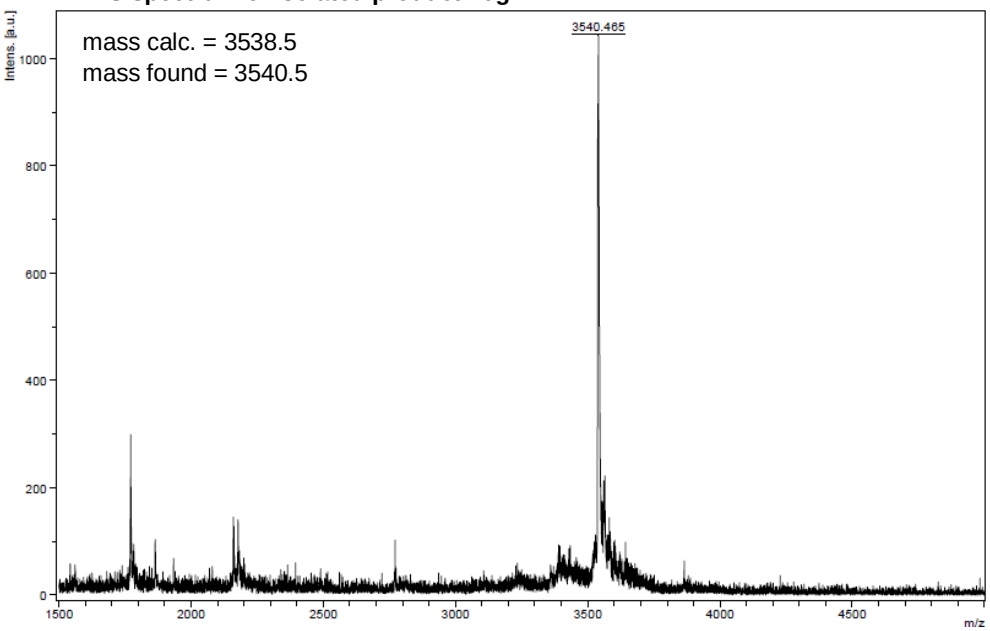
HPLC trace of isolated product 16g (Analytical RP-HPLC, Method-II)



Peak list:

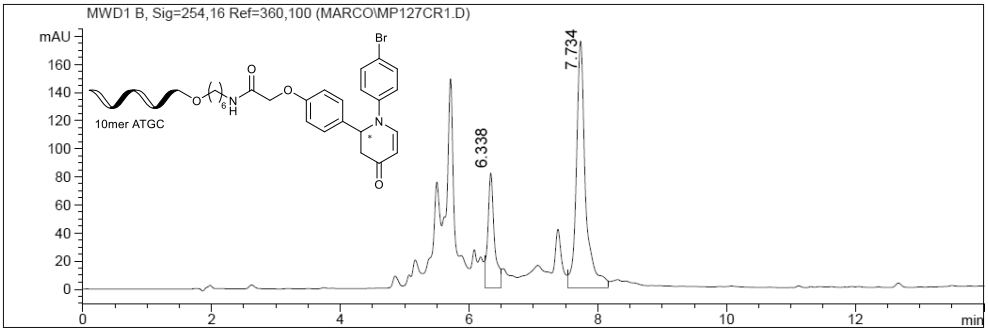
Ret. Time	Width min	Height	Area	Area %
7.318	0.147	229.286	2021.325	100.000

MALDI-MS spectrum of isolated product 16g



DNA conjugate 16h: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-bromoaniline **12h** and Danishefsky's diene **13** according to RP-07.

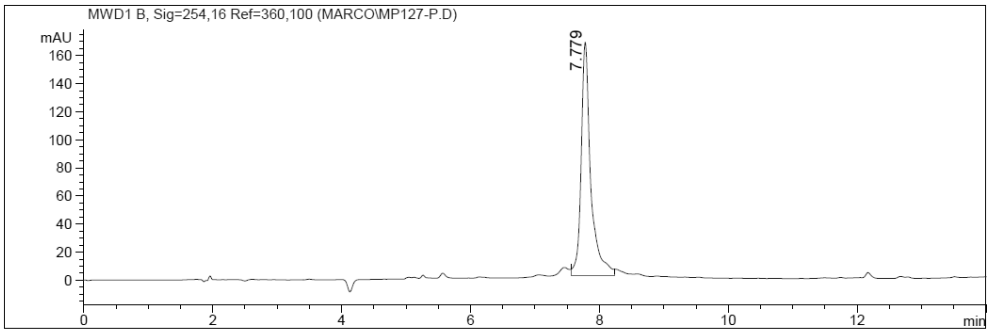
HPLC trace of crude reaction mixture 16h (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.338	0.117	81.814	572.011	24.990
7.734	0.163	175.931	1716.947	75.010

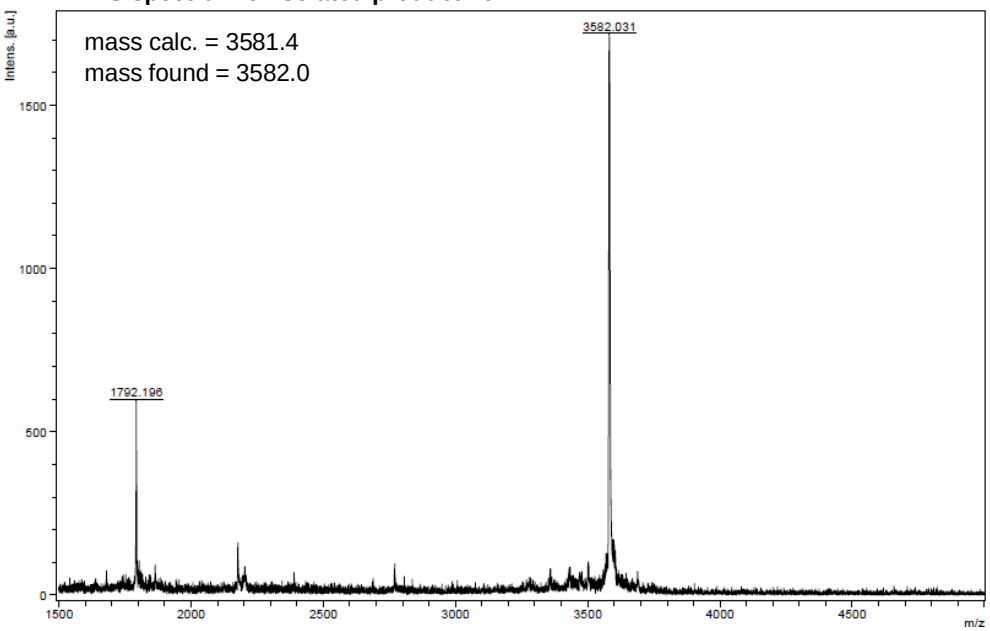
HPLC trace of isolated product 16h (Analytical RP-HPLC, Method-II)



Peak list:

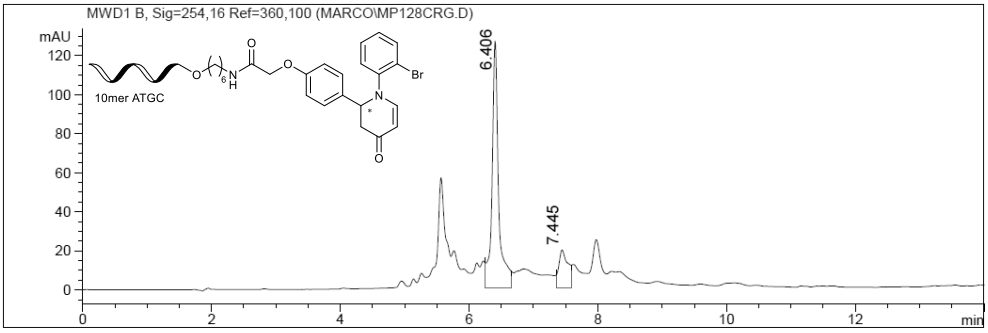
Ret. Time	Width min	Height	Area	Area %
7.779	0.173	166.620	1727.824	100.000

MALDI-MS spectrum of isolated product 16h



DNA conjugate 16i: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-bromoaniline **12i** and Danishefsky's diene **13** according to RP-07.

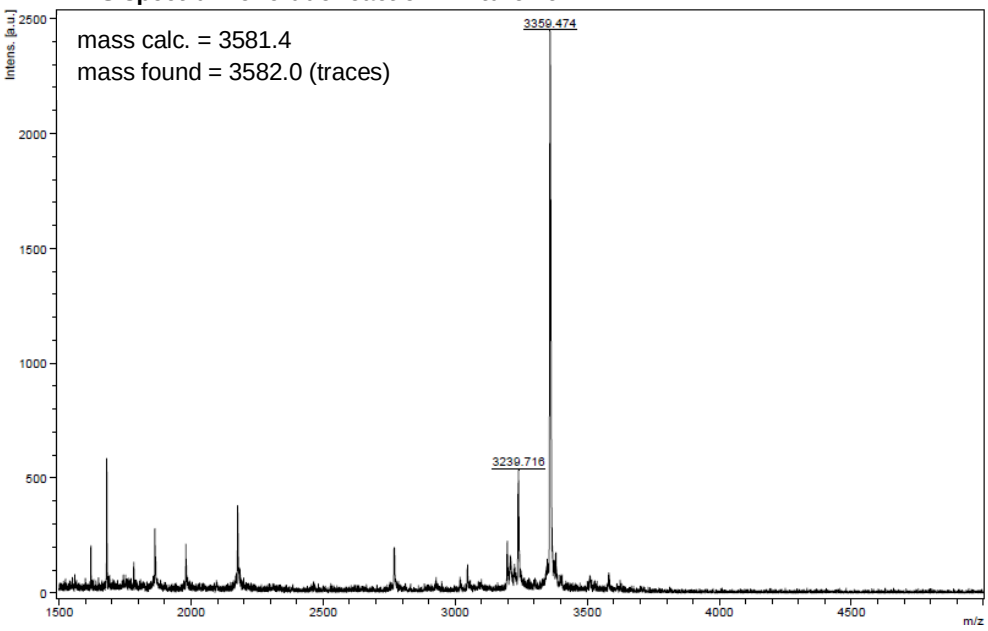
HPLC trace of crude reaction mixture 16i (Analytical RP-HPLC, Method-II)



Peak list:

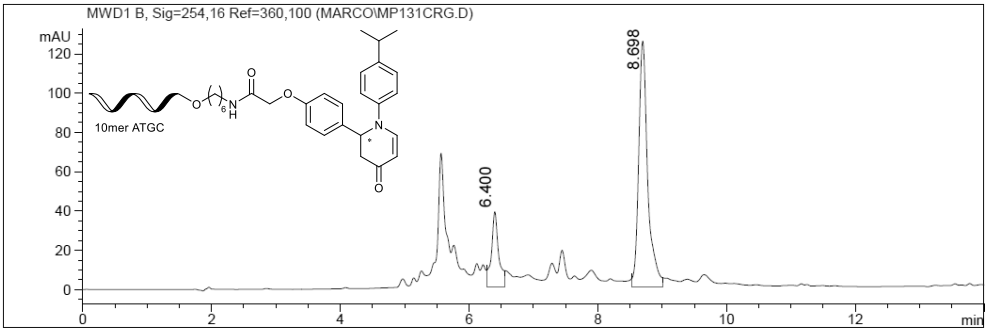
Ret. Time	Width min	Height	Area	Area %
6.406	0.117	126.845	892.818	82.131
7.445	0.165	19.606	194.252	17.869

MALDI-MS spectrum of crude reaction mixture 16i



DNA conjugate 16j: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-isopropylaniline **12j** and Danishefsky's diene **13** according to RP-07.

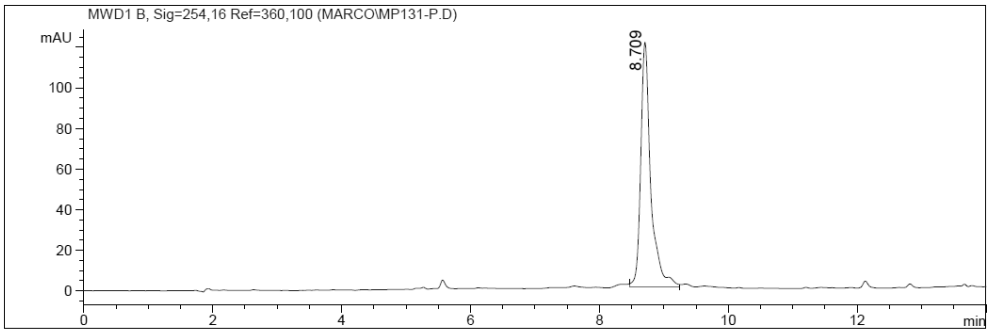
HPLC trace of crude reaction mixture 16j (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.400	0.130	38.296	299.374	19.818
8.698	0.161	125.035	1211.246	80.182

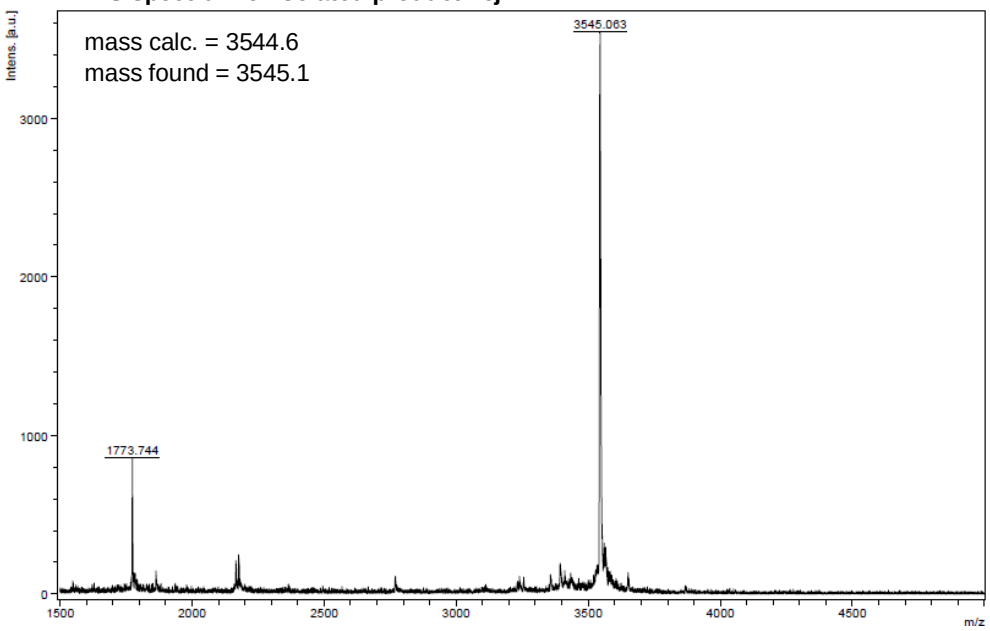
HPLC trace of isolated product 16j (Analytical RP-HPLC, Method-II)



Peak list:

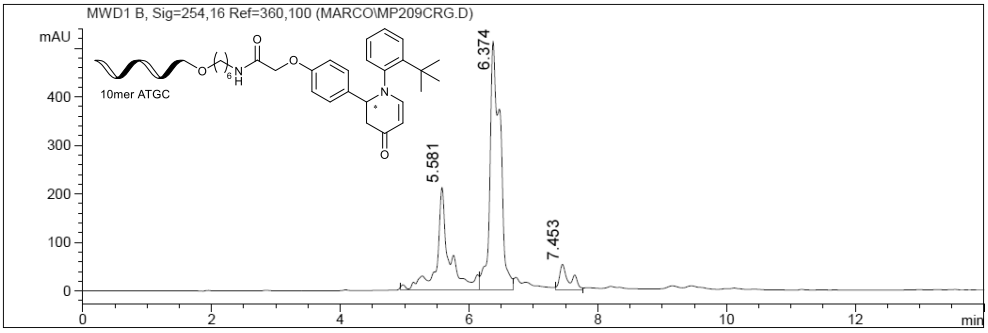
Ret. Time	Width min	Height	Area	Area %
8.709	0.180	120.773	1304.196	100.000

MALDI-MS spectrum of isolated product 16j



DNA conjugate 16k: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-*tert*-butylaniline **12k** and Danishefsky's diene **13** according to RP-07.

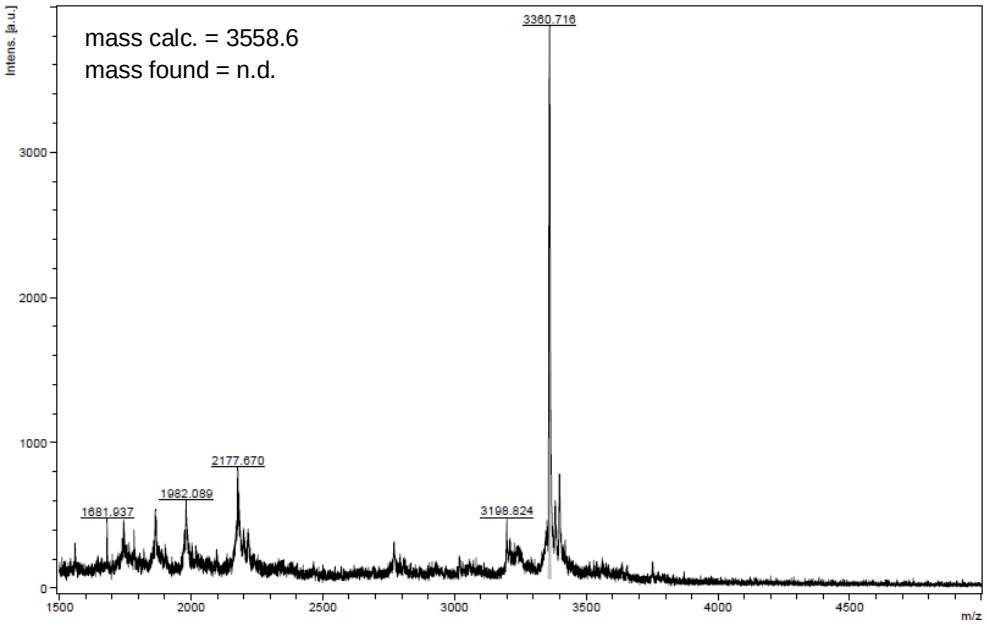
HPLC trace of crude reaction mixture 16k (Analytical RP-HPLC, Method-II)



Peak list:

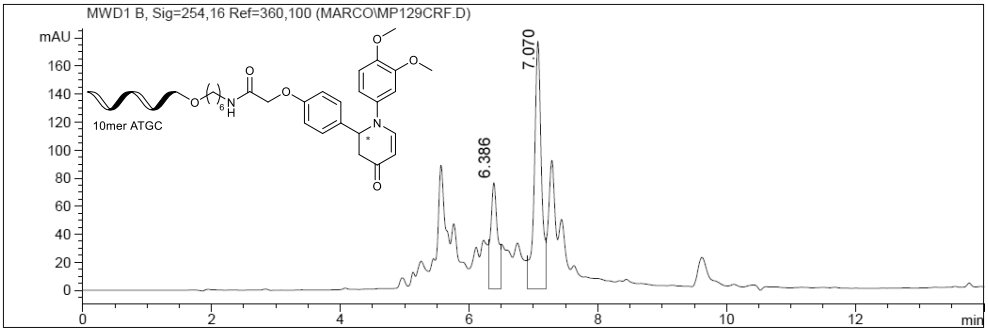
Ret. Time	Width min	Height	Area	Area %
5.581	0.228	211.424	2894.779	31.714
6.374	0.184	513.326	5666.833	62.083
7.453	0.180	52.493	566.200	6.203

MALDI-MS spectrum of crude reaction mixture 16k



DNA conjugate 16l: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3,4-dimethoxyaniline **12l** and Danishefsky's diene **13** according to RP-07.

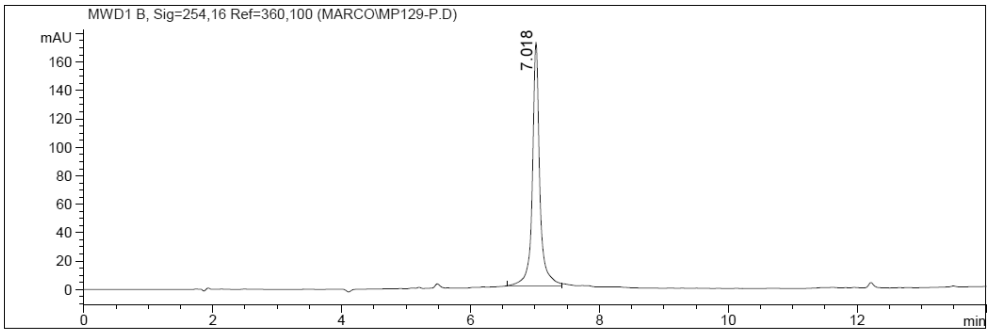
HPLC trace of crude reaction mixture 16l (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.386	0.122	75.789	554.931	29.066
7.070	0.128	176.746	1354.286	70.934

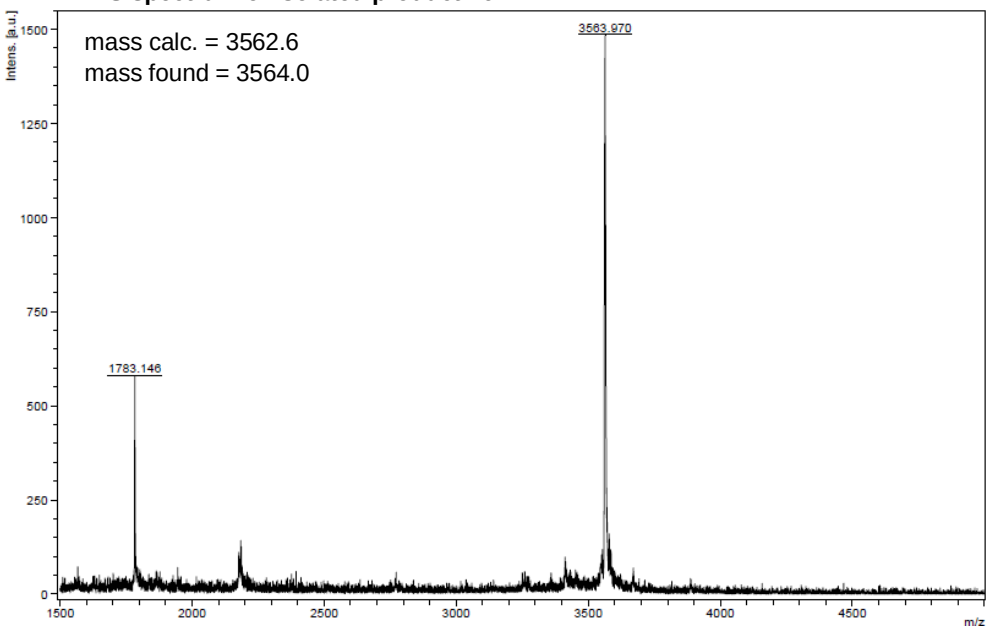
HPLC trace of isolated product 16l (Analytical RP-HPLC, Method-II)



Peak list:

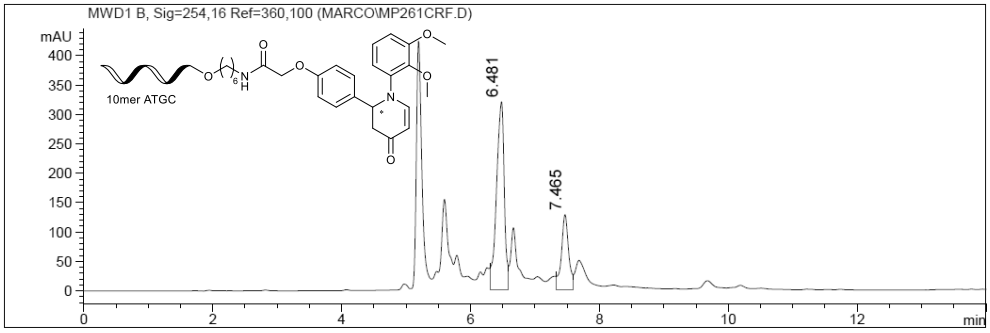
Ret. Time	Width min	Height	Area	Area %
7.018	0.134	171.713	1376.149	100.000

MALDI-MS spectrum of isolated product 16l



DNA conjugate 16m: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2,3-dimethoxyaniline **12m** and Danishefsky's diene **13** according to RP-07.

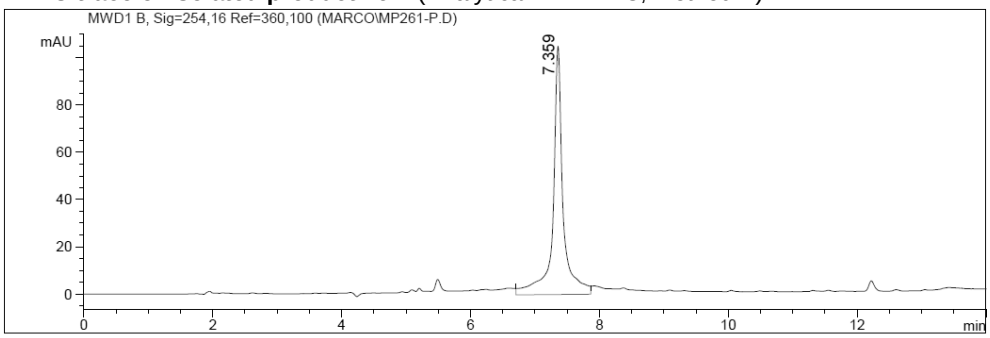
HPLC trace of crude reaction mixture 16m (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.481	0.139	320.999	2678.918	72.586
7.465	0.131	128.412	1011.742	27.414

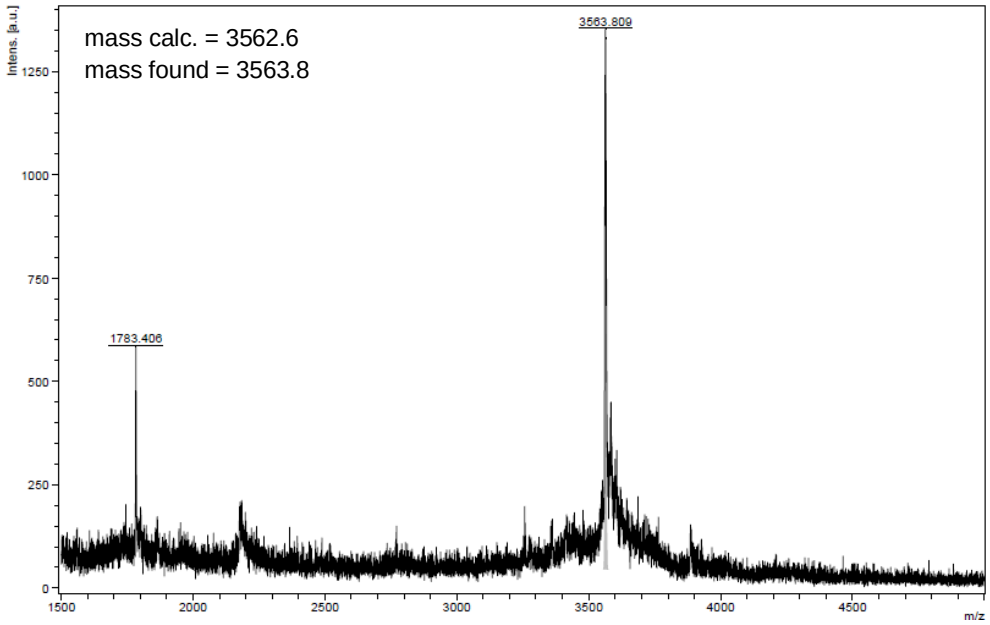
HPLC trace of isolated product 16m (Analytical RP-HPLC, Method-II)



Peak list:

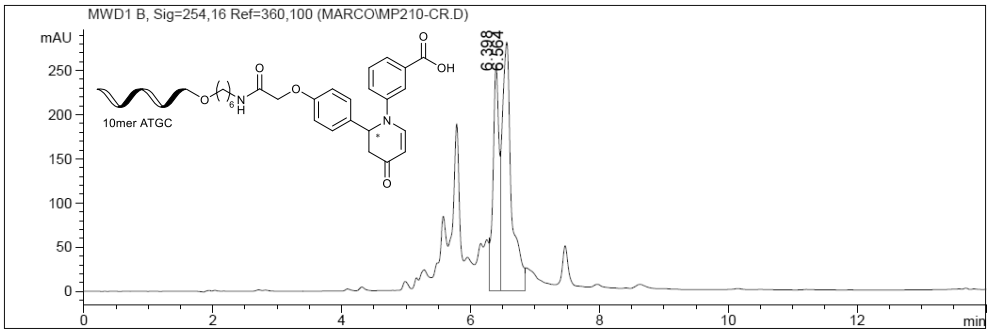
Ret. Time	Width min	Height	Area	Area %
7.359	0.151	104.883	1138.079	100.000

MALDI-MS spectrum of isolated product 16m



DNA conjugate 16n: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with methyl 3-aminobenzoate **12n** and Danishefsky's diene **13** according to RP-07.

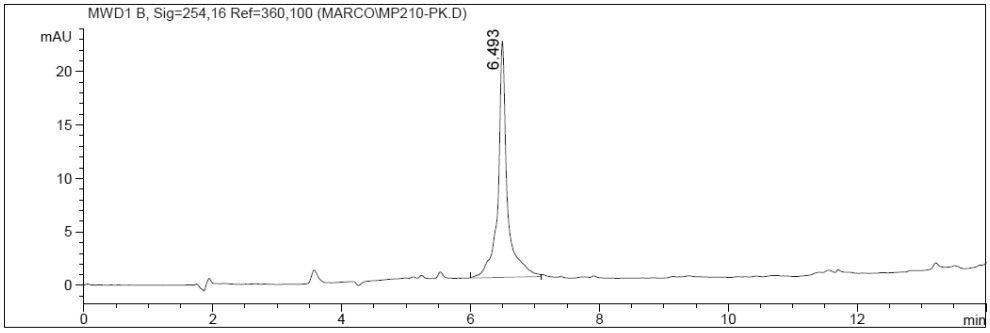
HPLC trace of crude reaction mixture 16n (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.398	0.104	255.696	1598.996	36.137
6.564	0.167	281.222	2825.759	63.863

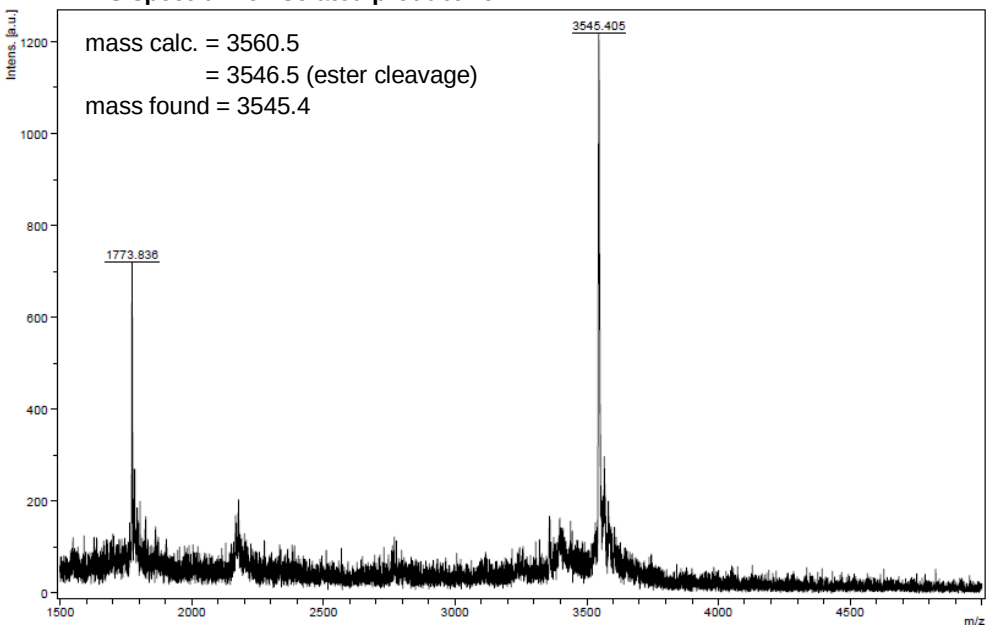
HPLC trace of isolated product 16n (Analytical RP-HPLC, Method-II)



Peak list:

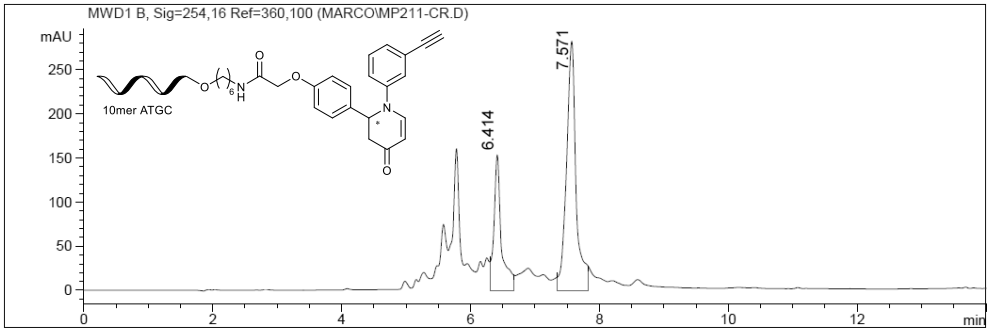
Ret. Time	Width min	Height	Area	Area %
6.493	0.137	22.085	217.159	100.000

MALDI-MS spectrum of isolated product 16n



DNA conjugate 16o: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-ethynylaniline **12o** and Danishefsky's diene **13** according to RP-07.

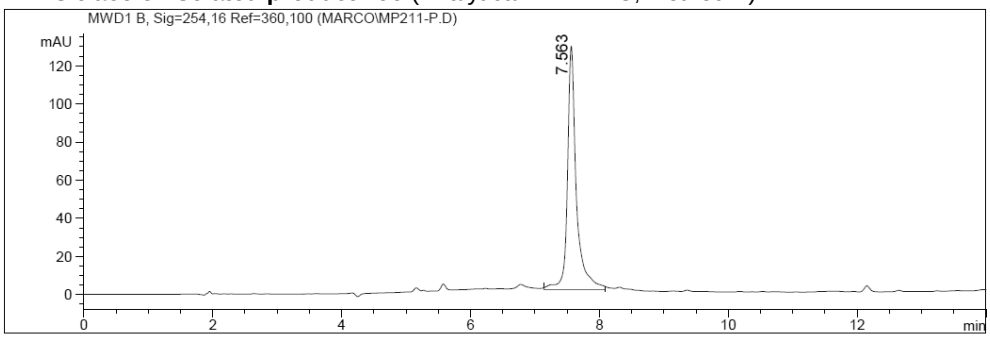
HPLC trace of crude reaction mixture 16o (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.414	0.137	154.339	1266.593	30.344
7.571	0.171	283.191	2907.571	69.656

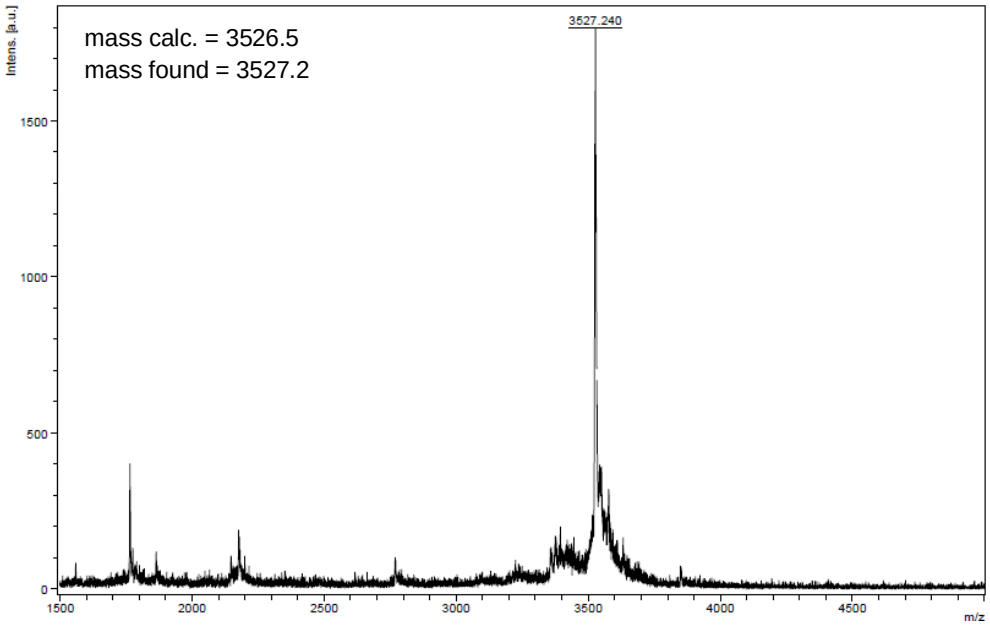
HPLC trace of isolated product 16o (Analytical RP-HPLC, Method-II)



Peak list:

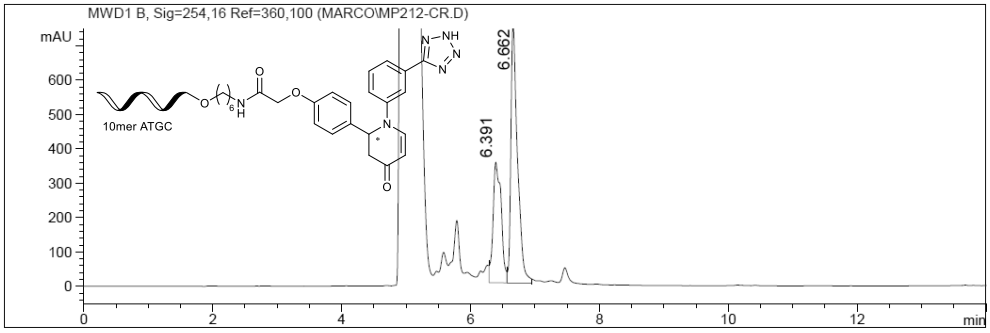
Ret. Time	Width min	Height	Area	Area %
7.563	0.160	127.921	1229.832	100.000

MALDI-MS spectrum of isolated product 16o



DNA conjugate 16p: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-(2H-tetrazol-5-yl)aniline **12p** and Danishefsky's diene **13** according to RP-07 (Dimethyl sulfoxide was used instead of acetonitrile).

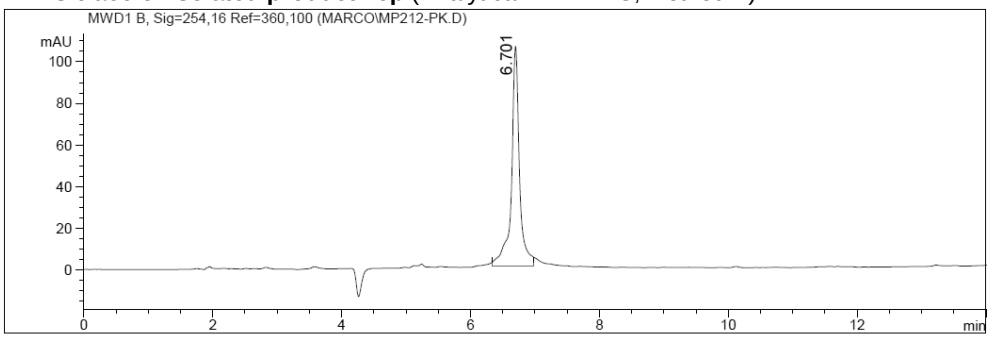
HPLC trace of crude reaction mixture 16p (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.391	0.147	351.703	3094.281	36.587
6.662	0.118	755.913	5362.938	63.413

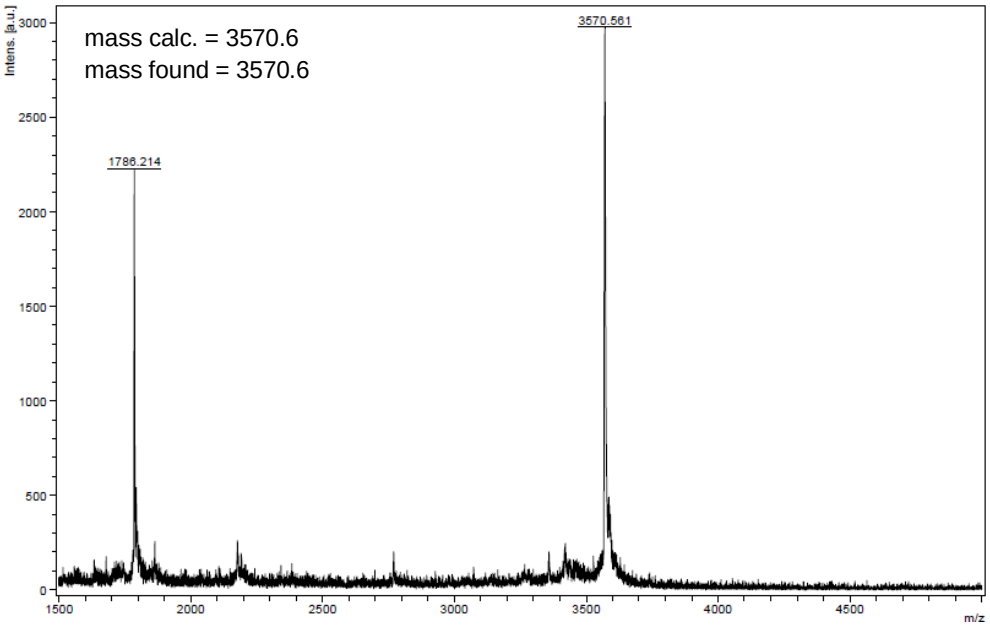
HPLC trace of isolated product 16p (Analytical RP-HPLC, Method-II)



Peak list:

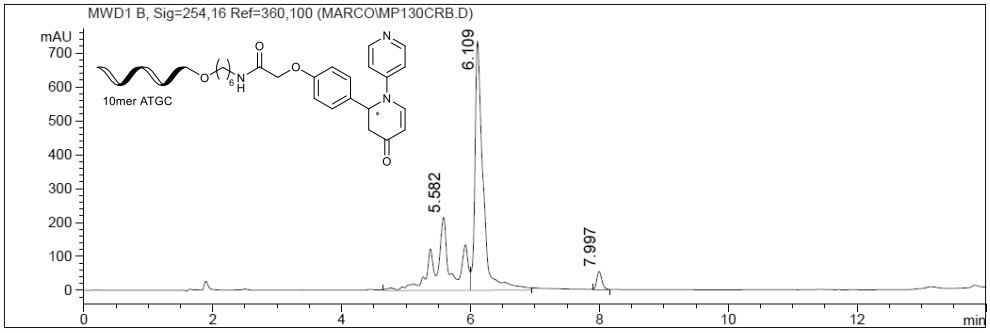
Ret. Time	Width min	Height	Area	Area %
6.701	0.147	105.983	932.071	100.000

MALDI-MS spectrum of isolated product 16p



DNA conjugate 16q: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with pyridin-4-amine **12q** and Danishefsky's diene **13** according to RP-07 (Dimethyl sulfoxide was used instead of acetonitrile).

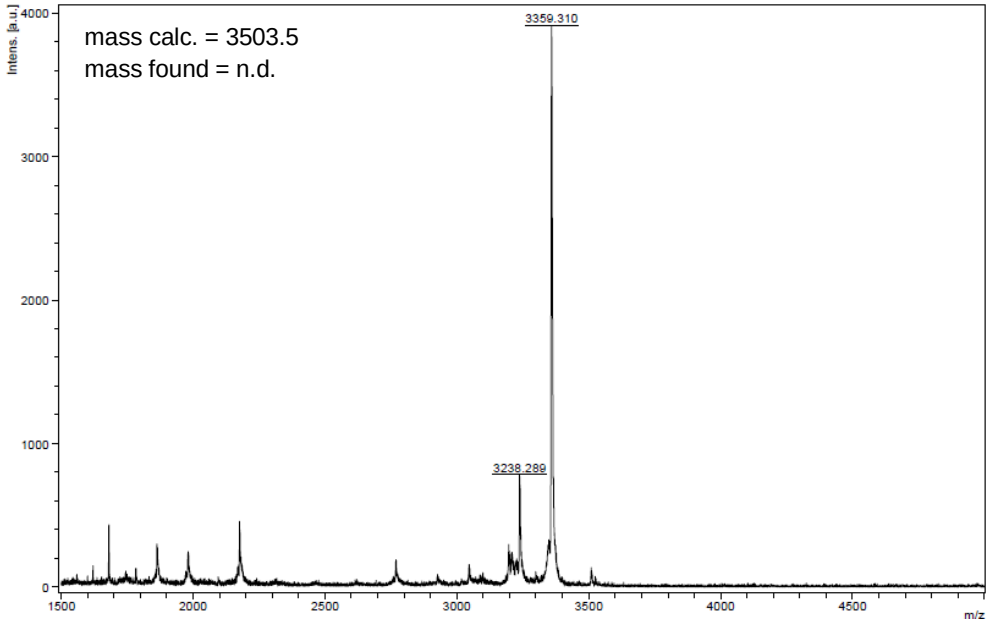
HPLC trace of crude reaction mixture 16q (Analytical RP-HPLC, Method-II)



Peak list:

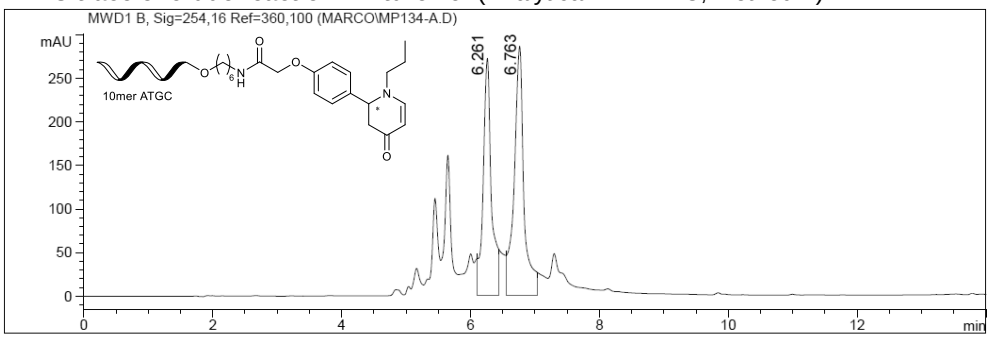
Ret. Time	Width min	Height	Area	Area %
5.582	0.307	215.698	3966.932	37.123
6.109	0.145	737.833	6401.872	59.910
7.997	0.096	54.891	317.055	2.967

MALDI-MS spectrum of crude reaction mixture 16q



DNA conjugate 16r: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with propylamine **12r** and Danishefsky's diene **13** according to RP-07 (1000 equiv. of amine were used, 100 equiv. of $Yb(OTf)_3$ were used instead of 50 equiv. of $ZnCl_2$).

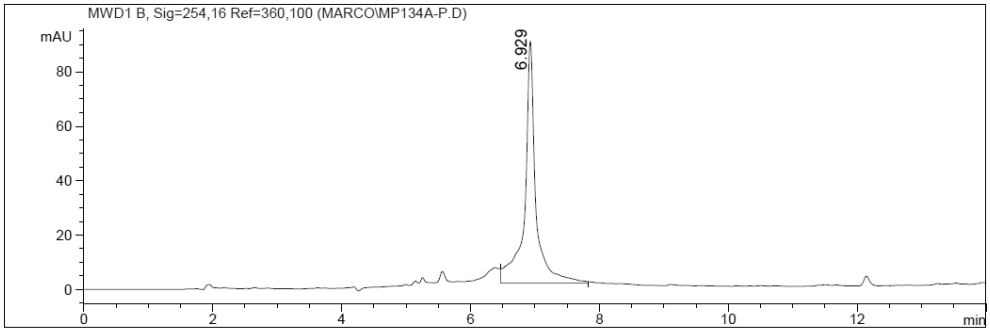
HPLC trace of crude reaction mixture 16r (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.261	0.147	271.945	2399.725	44.316
6.763	0.176	285.646	3015.307	55.684

HPLC trace of isolated product 16r (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.929	0.197	89.020	1053.850	100.000

MALDI-MS spectrum of isolated product 16r

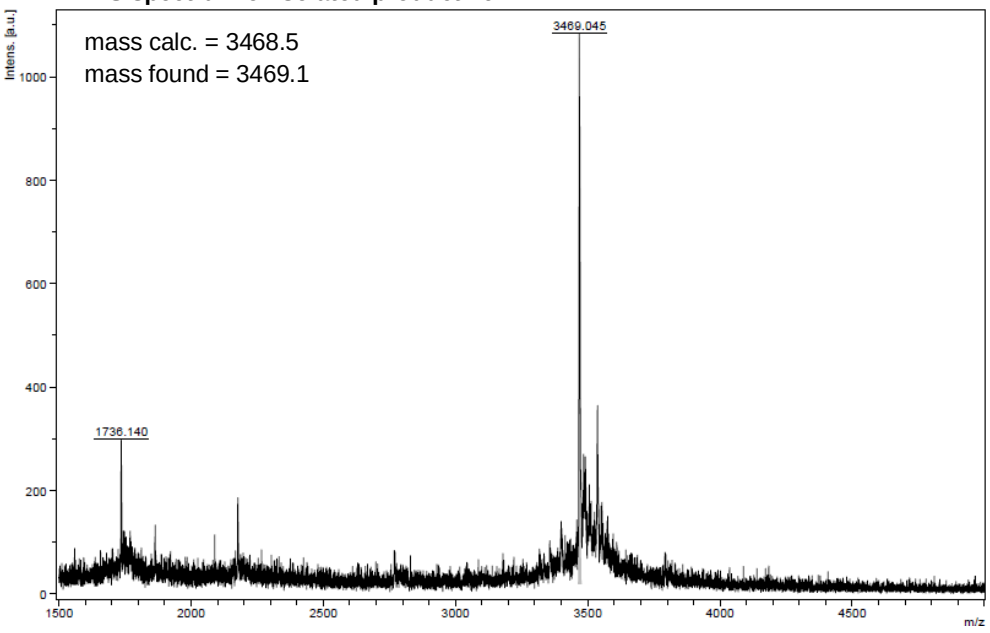
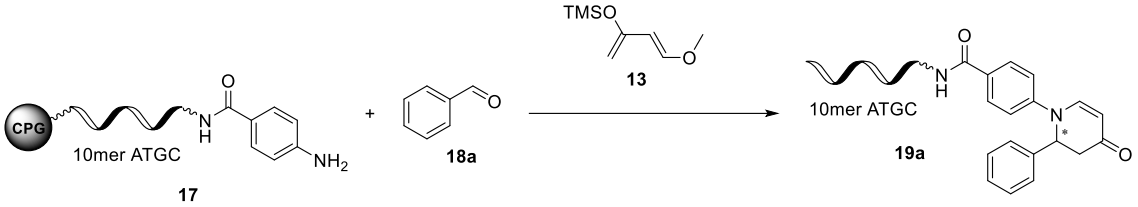
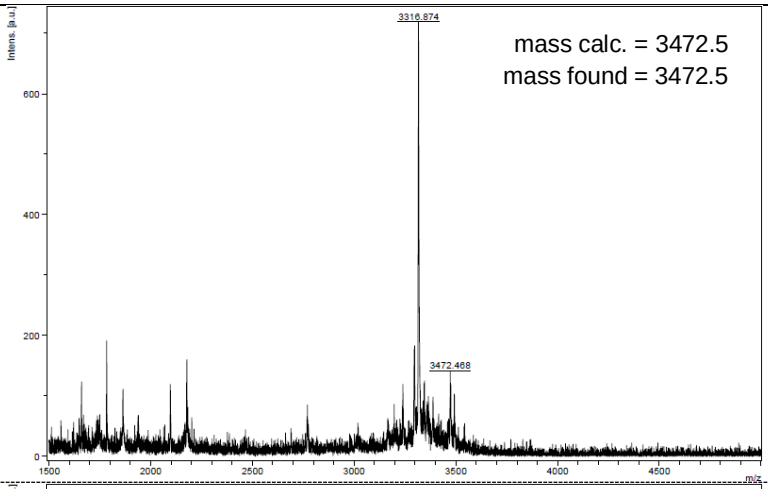
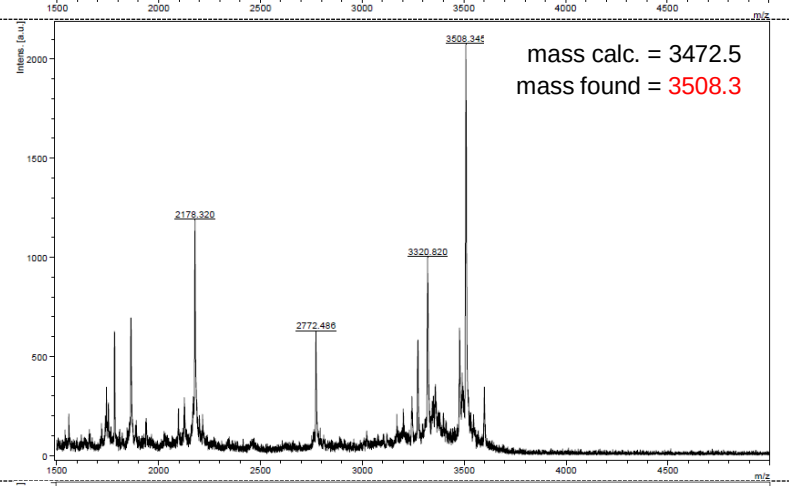
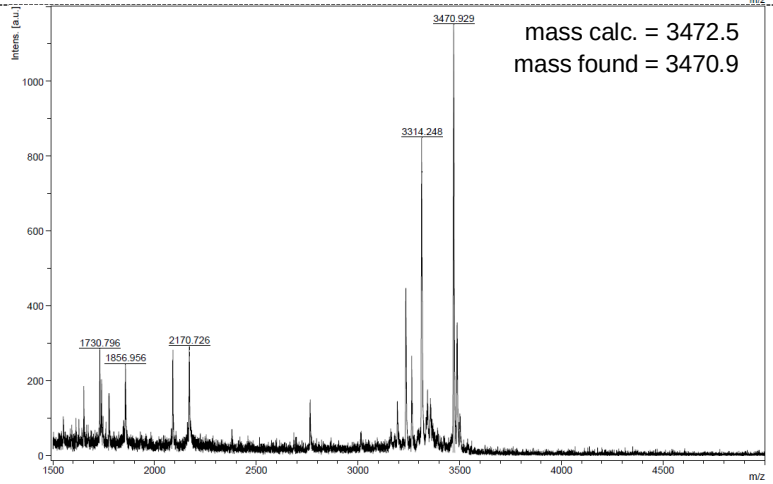


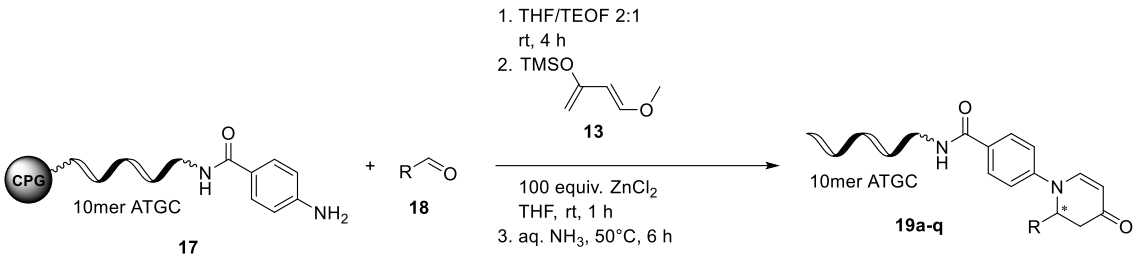
Table S7 Optimization of $ZnCl_2$-mediated aza-Diels-Alder reaction with benzaldehyde **18a** and Danishefsky's diene **13** on CPG-coupled 10mer ATGC oligonucleotide-aniline conjugate **17**.

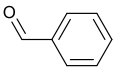
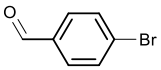
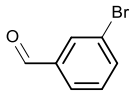
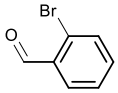
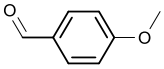
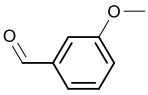
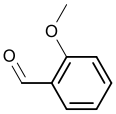
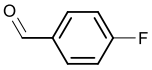
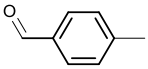
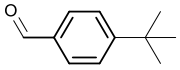
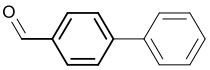
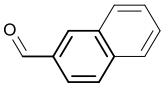


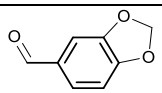
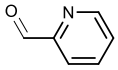
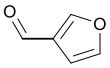
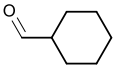
Entry	Reaction conditions[b]	MALDI MS spectra of crude reaction mixtures[c]
1	1. 500 equiv. **18a** ACN/TEOF (2:1), 4 h, rt 2. 1000 equiv. **13** 100 equiv. $ZnCl_2$ ACN, 1 h, rt 3. AMA, 4 h, rt => conversion: **traces**	
2	1. ***1500*** equiv. **18a** ***THF***/TEOF (2:1), 4 h, rt 2. 1000 equiv. **13** 100 equiv. $ZnCl_2$ ***THF***, 1 h, rt 3. AMA, 4 h, rt => conversion: ~ 60%	
3	1. 1500 equiv. **18a** THF/TEOF (2:1), 4 h, rt 2. 1000 equiv. **13** 100 equiv. $ZnCl_2$ THF, 1 h, rt 3. ***aq. 30% NH_3, 6 h, 50 °C*** => conversion: ~ 60%	

[a] Condensation of CPG-coupled 10mer ATGC-aniline conjugate **17** (20 nmol) with benzaldehyde **18a** (X equiv.) in 36 µL of indicated solvent/triethyl orthoformate (2:1) at ambient temperature for 4 h, then $ZnCl_2$ (100 equiv.) suspended in 30 µL of indicated solvent and Danishefsky's diene **13** (1000 equiv.) were added, the reaction mixture was shaken at ambient temperature for 1 h. [b] Changed parameters are in bold and italic. [c] Measured by MALDI-MS. 10mer ATGC = 5'-GTC ATG ATC T-3'. n.d. = not detected. TEOF = triethyl orthoformate.

Table S8 – Scope of $ZnCl_2$-mediated aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled 10mer ATGC oligonucleotide-aniline conjugate using different aldehydes.[a]



Entry	Product	Aldehyde	Conversion [%][b]	Mass$_{calc.}$ Mass$_{found}$[c]
1	**19a**	 **18a**	62	3472.5 3473.3
2	**19b**	 **18b**	60	3551.4 3552.4
3	**19c**	 **18c**	64	3551.4 3552.5
4	**19d**	 **18d**	56	3551.4 3551.3
5	**19e**	 **18e**	58	3502.5 3502.8
6	**19f**	 **18f**	71	3502.5 3503.2
7	**19g**	 **18g**	64	3502.5 3503.2
8	**19h**	 **18h**	58	3490.5 3491.7
9	**19i**	 **18i**	57	3486.5 3488.4
10	**19j**	 **18j**	50	3528.6 3529.0
11	**19k**	 **18k**	65	3548.6 3549.0
12	**19l**	 **18l**	60	3522.5 3524.1

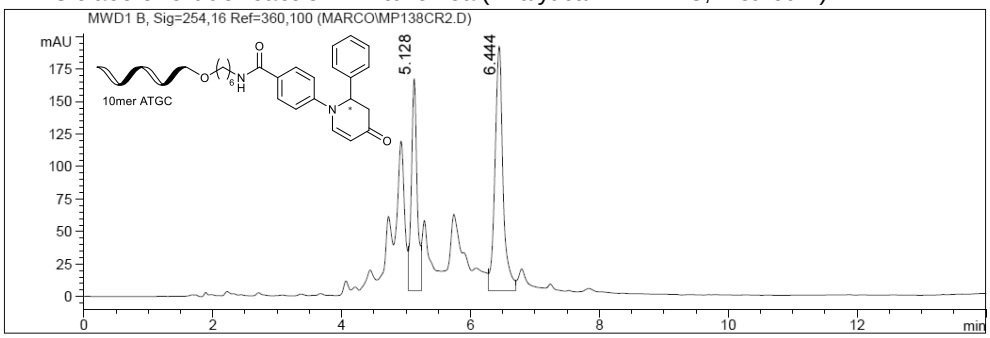
13	**19m**	 **18m**	48	3516.5 3518.6
14	**19n**	 **18n**	38	3473.5 3474.8
15	**19o**	 **18o**	56	3462.4 3464.1
16	**19p**	 **18p**	34	3478.5 3478.5
17	**19q**	 **18q**	18	3438.5 3437.0

[a] Condensation of CPG-coupled oligonucleotide conjugate **17** (20 nmol) with aldehyde **18** (1500 equiv., 30 µmol) in 36 µL tetrahydrofuran/triethyl orthoformate (2:1) at ambient temperature for 4 h, then addition of $ZnCl_2$ (100 equiv., 2 µmol) dissolved in 30 µL tetrahydrofuran and Danishefsky's diene **15** (1000 equiv., 20 µmol) at ambient temperature for 1 h. DNA cleavage with 30 % aqueous ammonia at 50 °C for 6 h. [b] Determined by analytical RP-HPLC analysis. [c] Measured by MALDI-MS. 10mer ATGC = 5'-GTC ATG ATC T-3'. n.d. = not detected.

Products of aza-Diels-Alder reaction with Danishefsky's diene on CPG-coupled 10mer ATGC oligonucleotide-aniline conjugate

DNA conjugate 19a: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with benzaldehyde **18a** and Danishefsky's diene **13** according to RP-08.

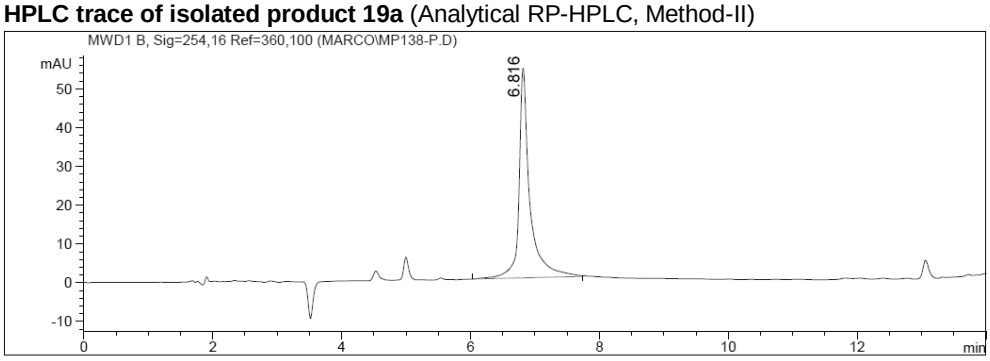
HPLC trace of crude reaction mixture 19a (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.128	0.101	163.317	993.368	37.589
6.444	0.146	188.069	1649.351	62.411

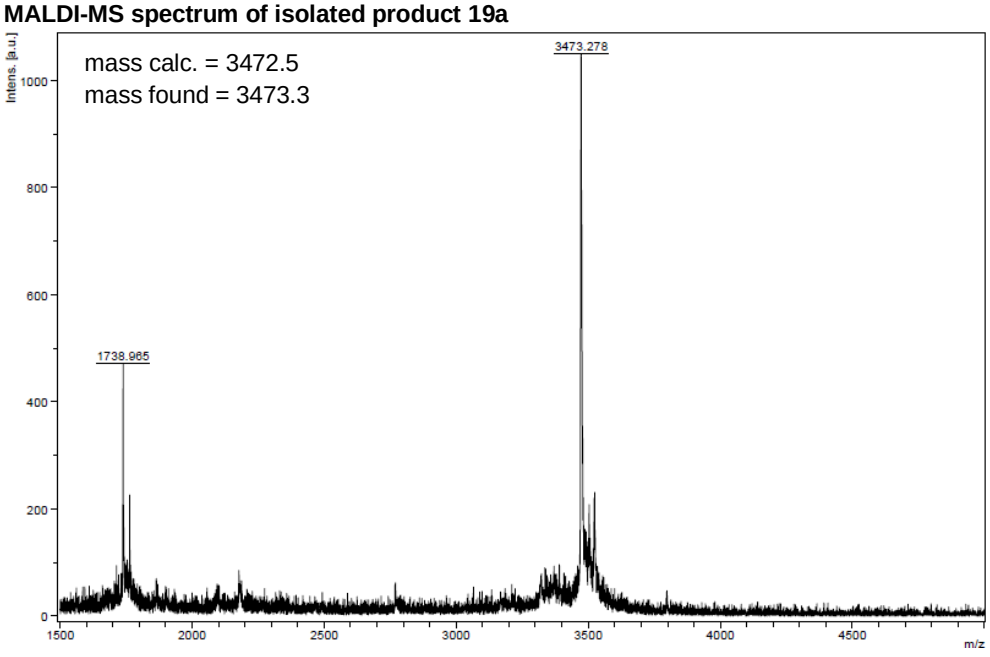
HPLC trace of isolated product 19a (Analytical RP-HPLC, Method-II)



Peak list:

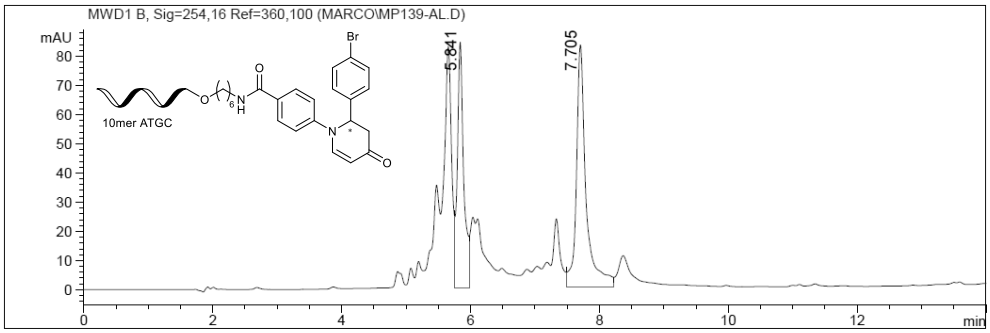
Ret. Time	Width min	Height	Area	Area %
6.816	0.164	54.110	632.311	100.000

MALDI-MS spectrum of isolated product 19a



DNA conjugate 19b: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 4-bromobenzaldehyde **18b** and Danishefsky's diene **13** according to RP-08.

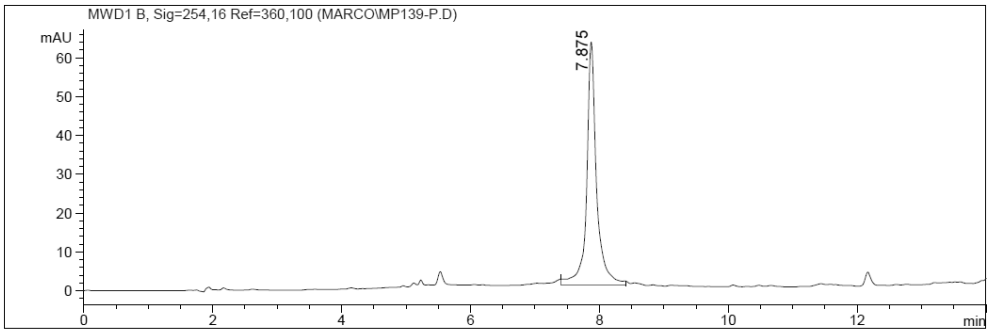
HPLC trace of crude reaction mixture 19b (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.841	0.113	84.160	571.159	39.796
7.705	0.173	83.182	864.044	60.204

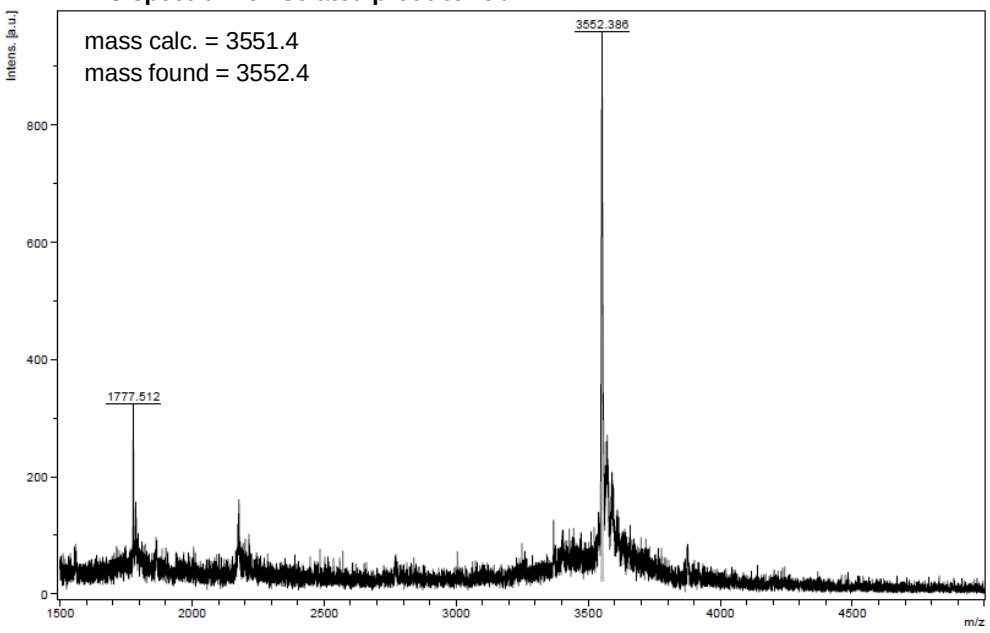
HPLC trace of isolated product 19b (Analytical RP-HPLC, Method-II)



Peak list:

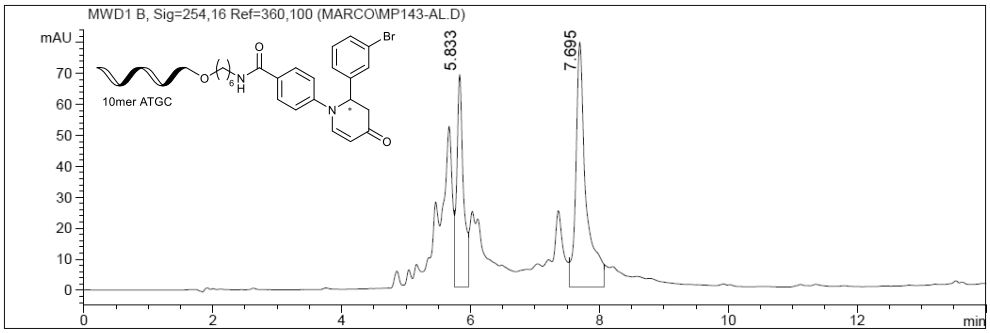
Ret. Time	Width min	Height	Area	Area %
7.875	0.177	62.652	664.216	100.000

MALDI-MS spectrum of isolated product 19b



DNA conjugate 19c: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 3-bromobenzaldehyde **18c** and Danishefsky's diene **13** according to RP-08.

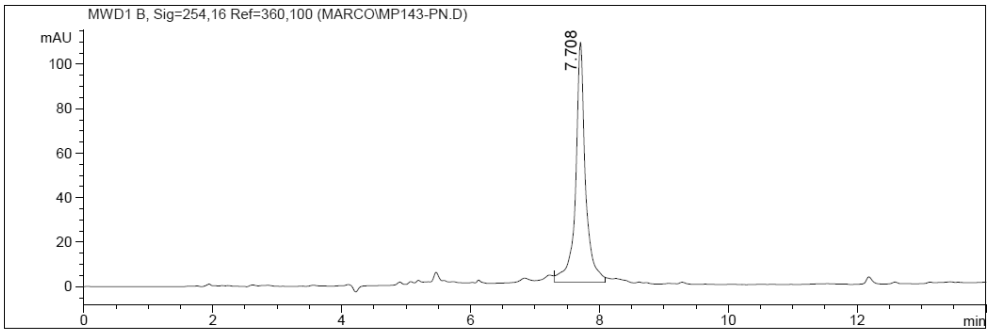
HPLC trace of crude reaction mixture 19c (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.833	0.117	68.815	484.264	35.791
7.695	0.183	79.125	868.751	64.209

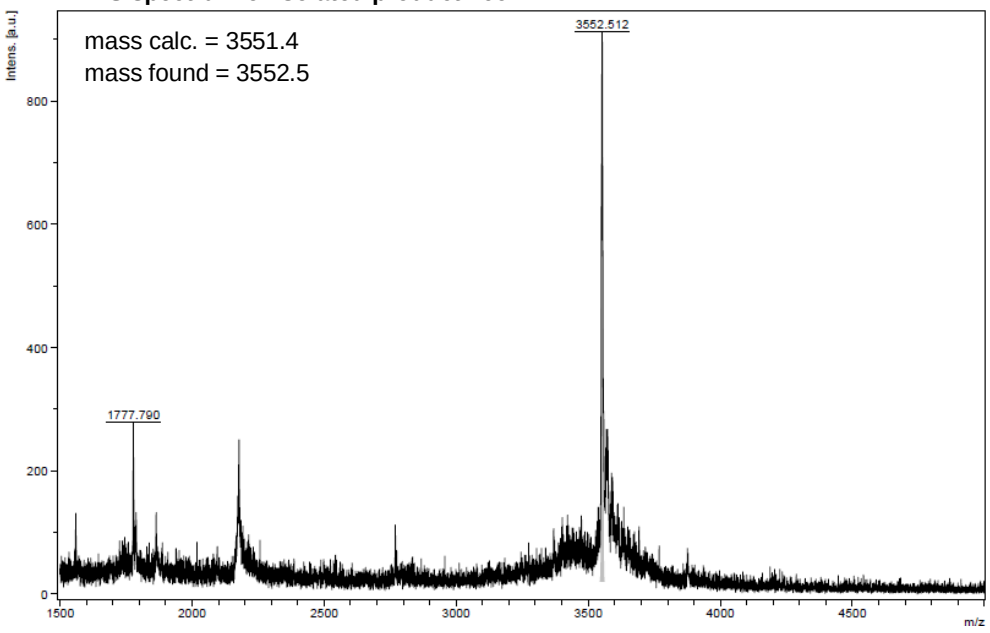
HPLC trace of isolated product 19c (Analytical RP-HPLC, Method-II)



Peak list:

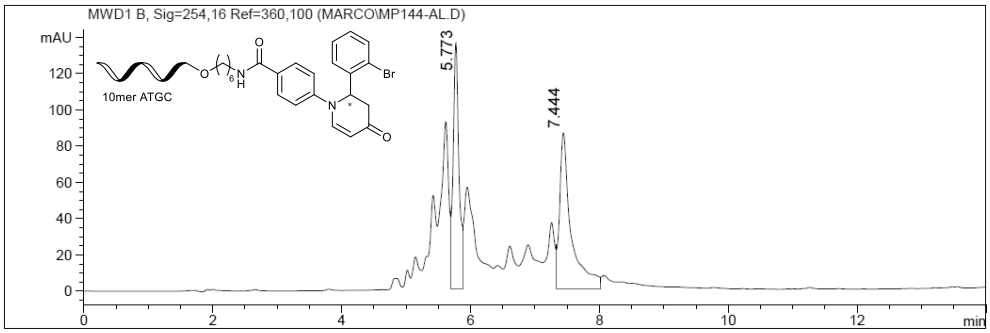
Ret. Time	Width min	Height	Area	Area %
7.708	0.177	108.018	1146.097	100.000

MALDI-MS spectrum of isolated product 19c



DNA conjugate 19d: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 2-bromobenzaldehyde **18d** and Danishefsky's diene **13** according to RP-08.

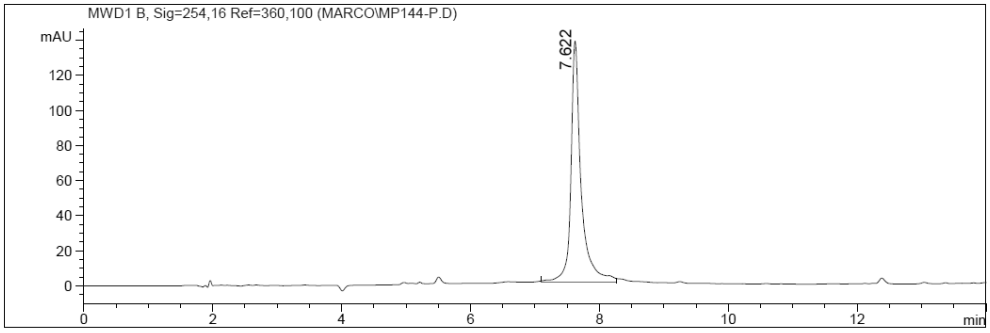
HPLC trace of crude reaction mixture 19d (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.773	0.103	136.557	840.018	43.548
7.444	0.210	86.380	1088.924	56.452

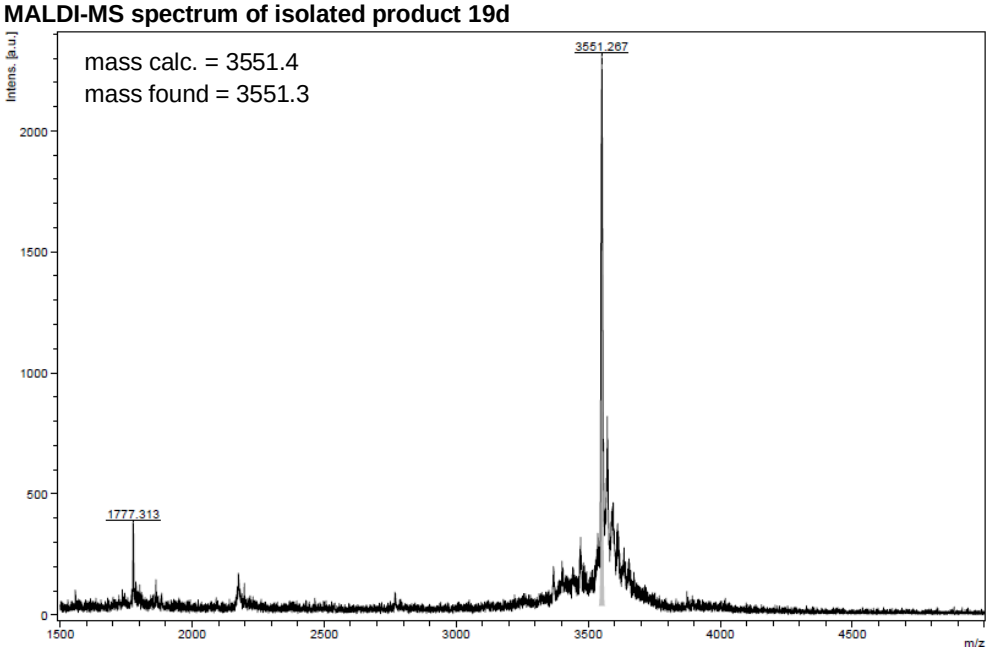
HPLC trace of isolated product 19d (Analytical RP-HPLC, Method-II)



Peak list:

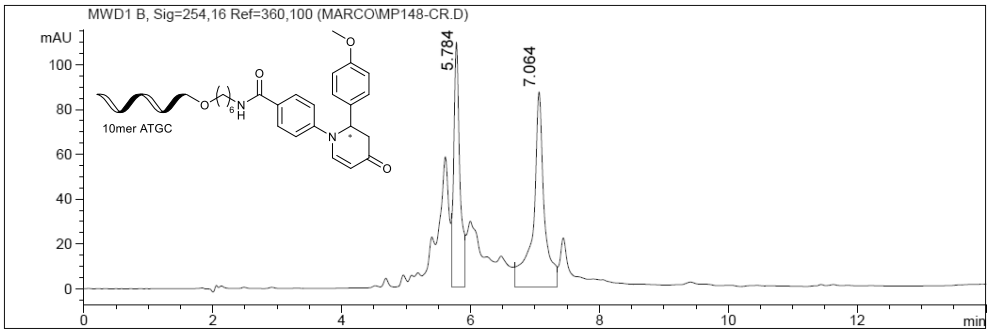
Ret. Time	Width min	Height	Area	Area %
7.622	0.185	137.808	1527.506	100.000

MALDI-MS spectrum of isolated product 19d



DNA conjugate 19e: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 4-methoxybenzaldehyde **18e** and Danishefsky's diene **13** according to RP-08.

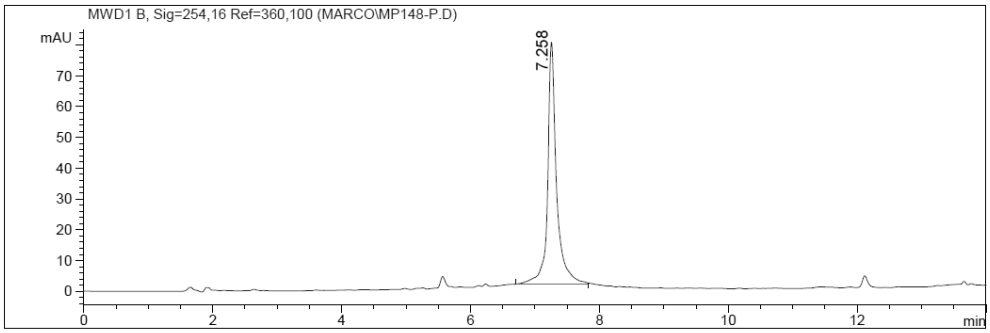
HPLC trace of crude reaction mixture 19e (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.784	0.111	109.344	725.500	41.666
7.064	0.194	87.057	1015.736	58.334

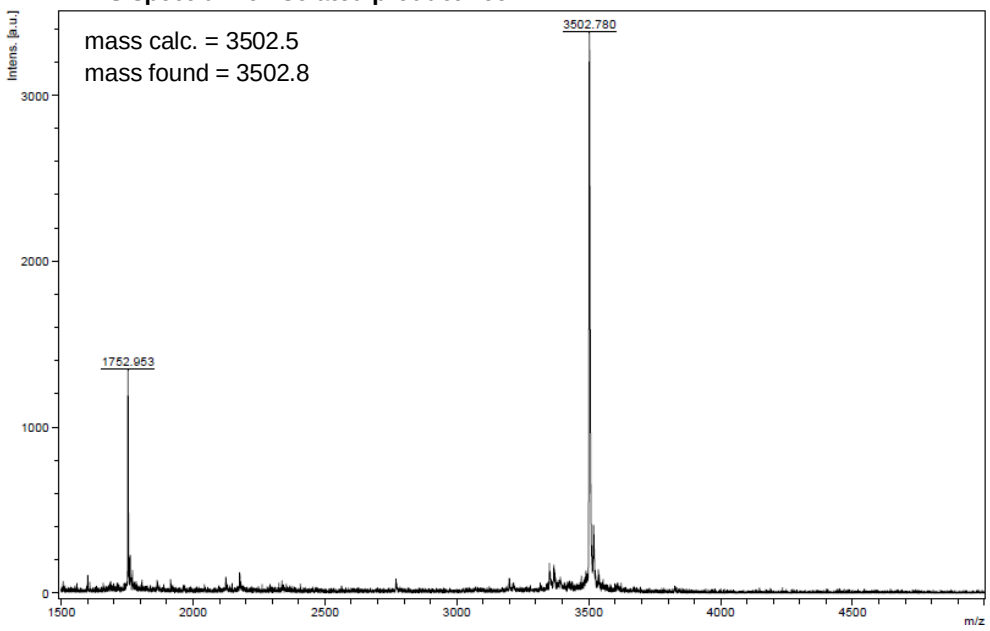
HPLC trace of isolated product 19e (Analytical RP-HPLC, Method-II)



Peak list:

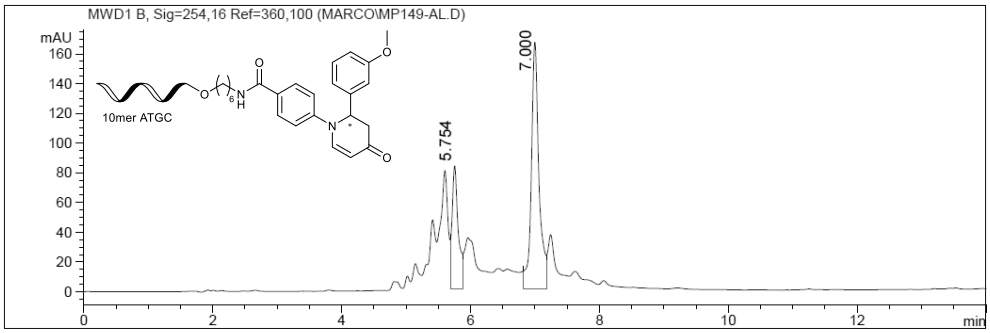
Ret. Time	Width min	Height	Area	Area %
7.258	0.162	78.696	763.349	100.000

MALDI-MS spectrum of isolated product 19e



DNA conjugate 19f: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 3-methoxybenzaldehyde **18f** and Danishefsky's diene **13** according to RP-08.

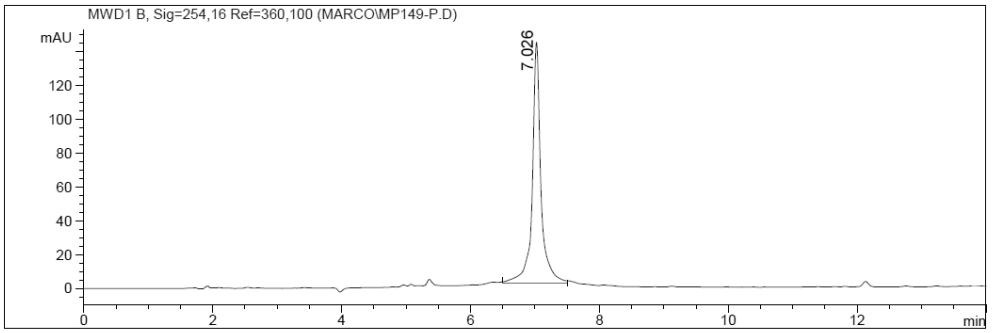
HPLC trace of crude reaction mixture 19f (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.754	0.111	83.312	555.542	28.989
7.000	0.136	166.735	1360.813	71.011

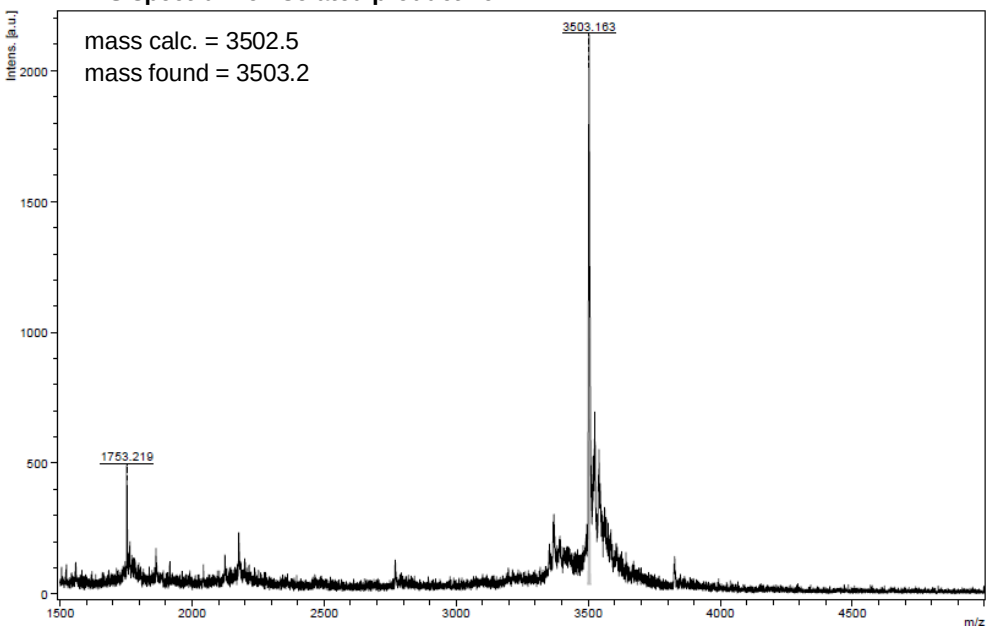
HPLC trace of isolated product 19f (Analytical RP-HPLC, Method-II)



Peak list:

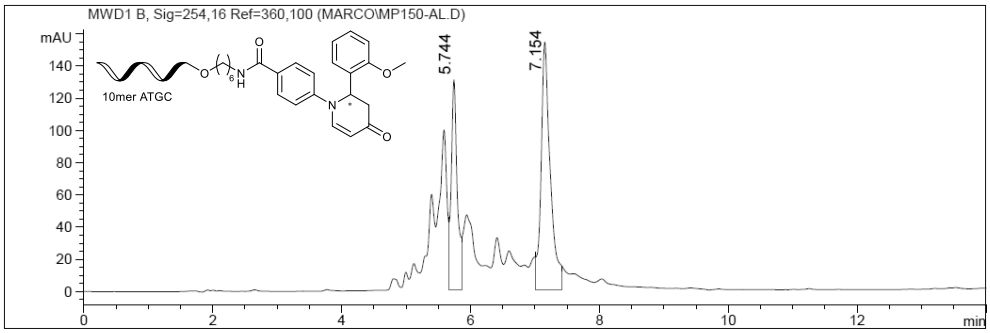
Ret. Time	Width min	Height	Area	Area %
7.026	0.155	142.647	1325.466	100.000

MALDI-MS spectrum of isolated product 19f



DNA conjugate 19g: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 2-methoxybenzaldehyde **18g** and Danishefsky's diene **13** according to RP-08.

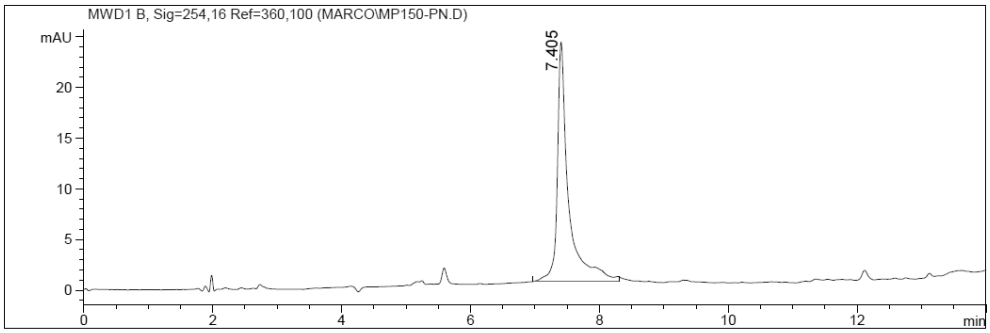
HPLC trace of crude reaction mixture 19g (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.744	0.108	130.706	845.267	35.788
7.154	0.164	154.065	1516.604	64.212

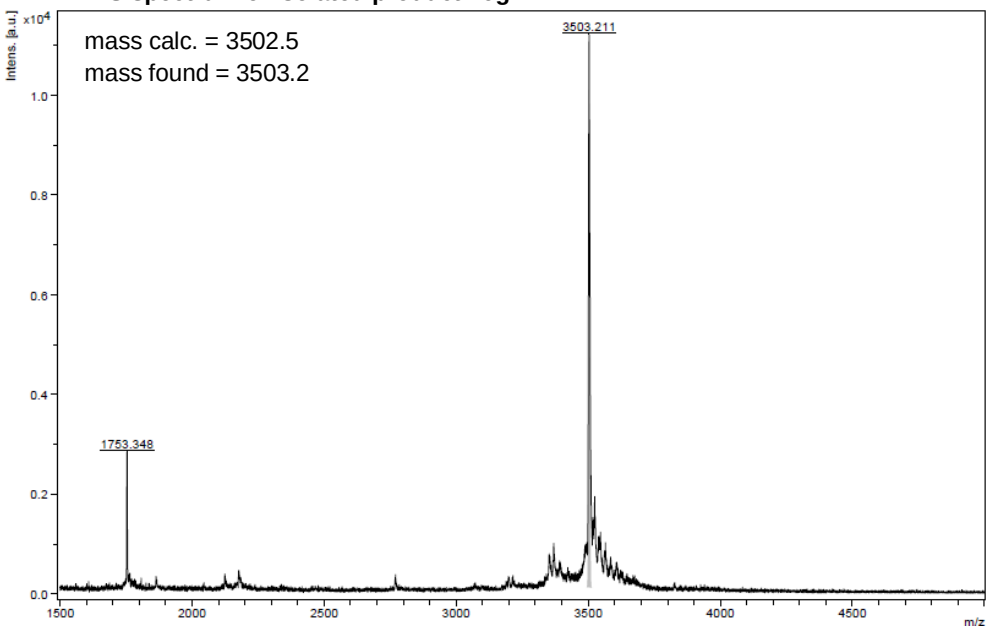
HPLC trace of isolated product 19g (Analytical RP-HPLC, Method-II)



Peak list:

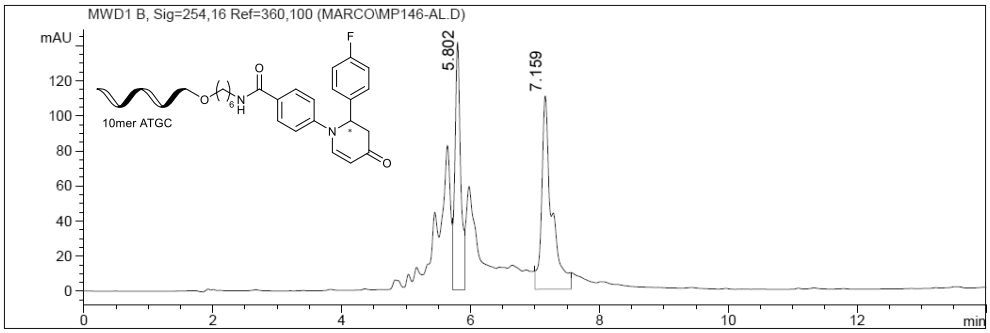
Ret. Time	Width min	Height	Area	Area %
7.405	0.201	23.642	285.662	100.000

MALDI-MS spectrum of isolated product 19g



DNA conjugate 19h: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 4-fluorobenzaldehyde **18h** and Danishefsky's diene **13** according to RP-08.

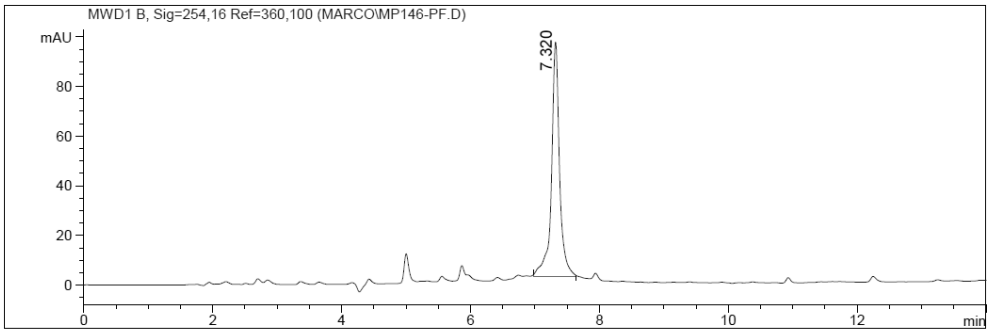
HPLC trace of crude reaction mixture 19h (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.802	0.100	141.245	847.449	41.605
7.159	0.180	110.390	1189.461	58.395

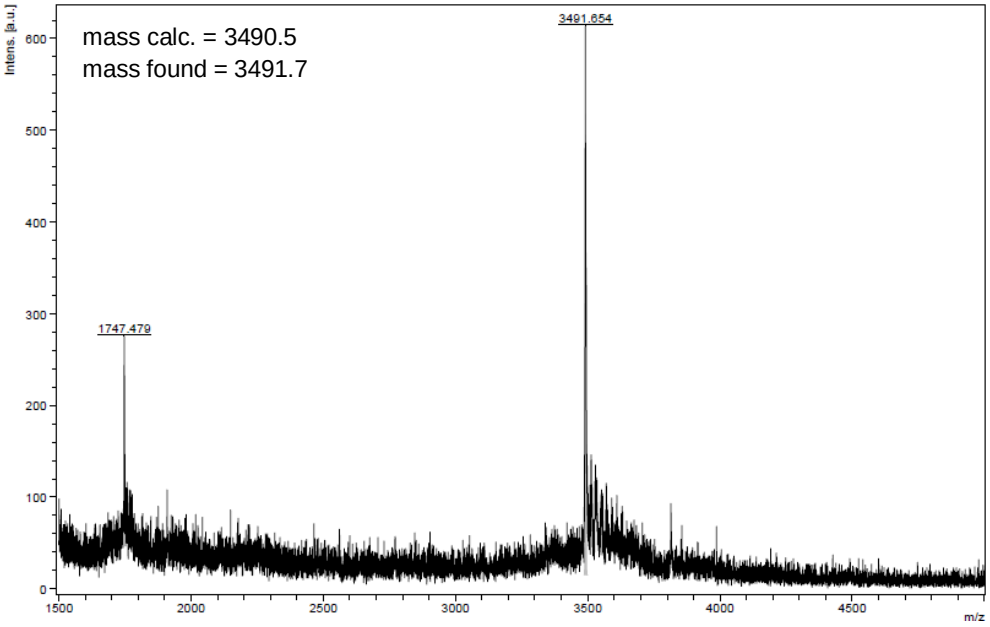
HPLC trace of isolated product 19h (Analytical RP-HPLC, Method-II)



Peak list:

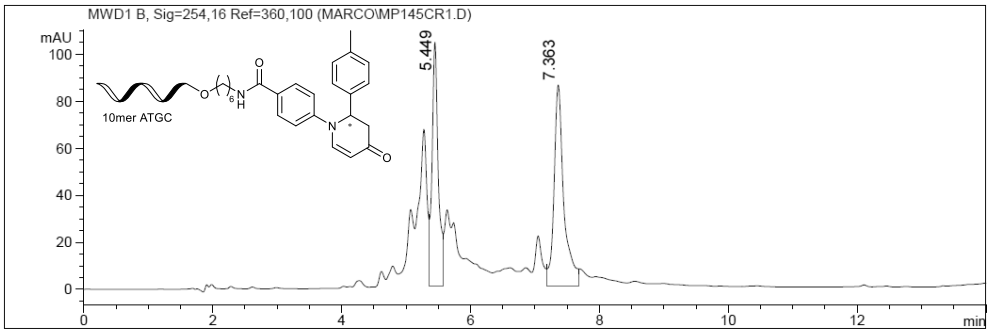
Ret. Time	Width min	Height	Area	Area %
7.320	0.145	94.654	824.639	100.000

MALDI-MS spectrum of isolated product 19h



DNA conjugate 19i: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 4-methylbenzaldehyde **18i** and Danishefsky's diene **13** according to RP-08.

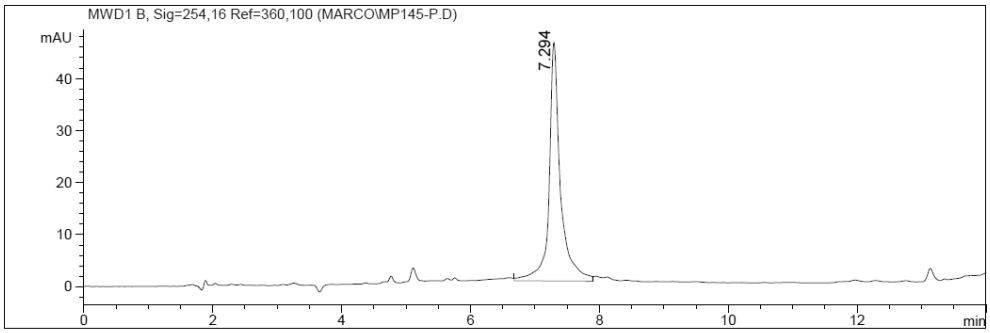
HPLC trace of crude reaction mixture 19i (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.449	0.110	104.130	688.043	43.079
7.363	0.177	85.811	909.125	56.921

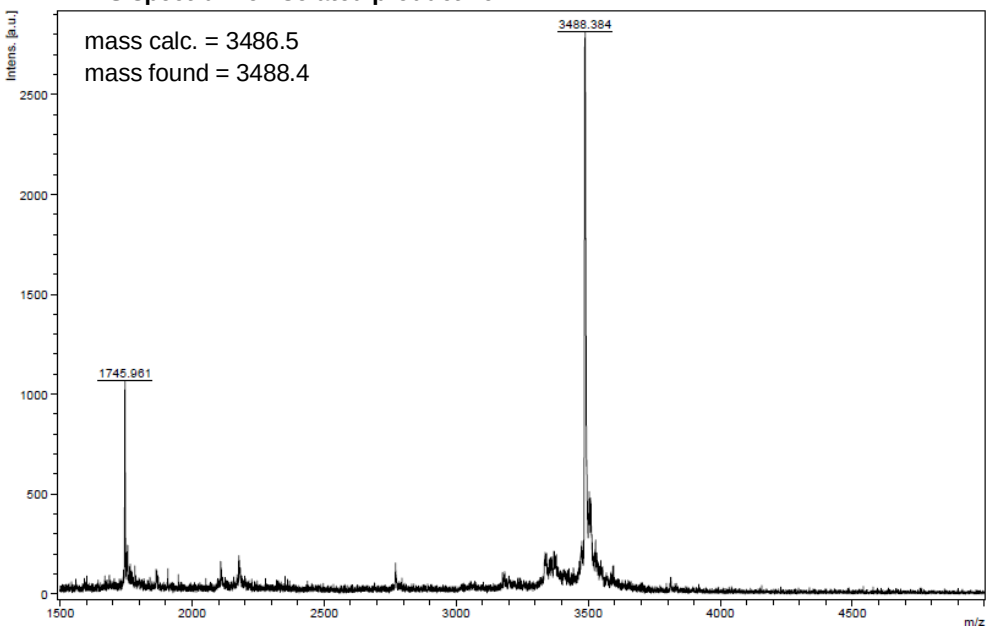
HPLC trace of isolated product 19i (Analytical RP-HPLC, Method-II)



Peak list:

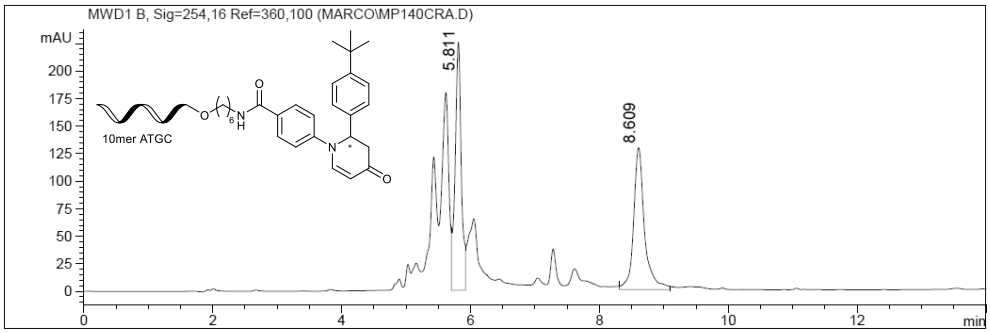
Ret. Time	Width min	Height	Area	Area %
7.294	0.173	45.899	564.514	100.000

MALDI-MS spectrum of isolated product 19i



DNA conjugate 19j: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 4-*tert*-butylbenzaldehyde **18j** and Danishefsky's diene **13** according to RP-08.

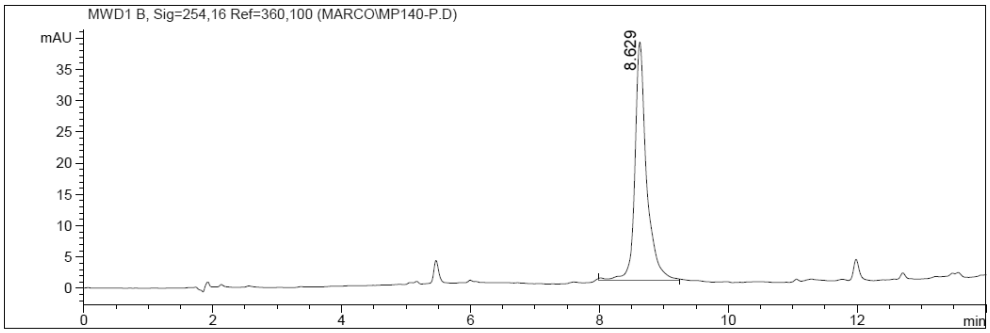
HPLC trace of crude reaction mixture 19j (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.811	0.111	225.544	1505.354	49.837
8.609	0.196	128.977	1515.207	50.163

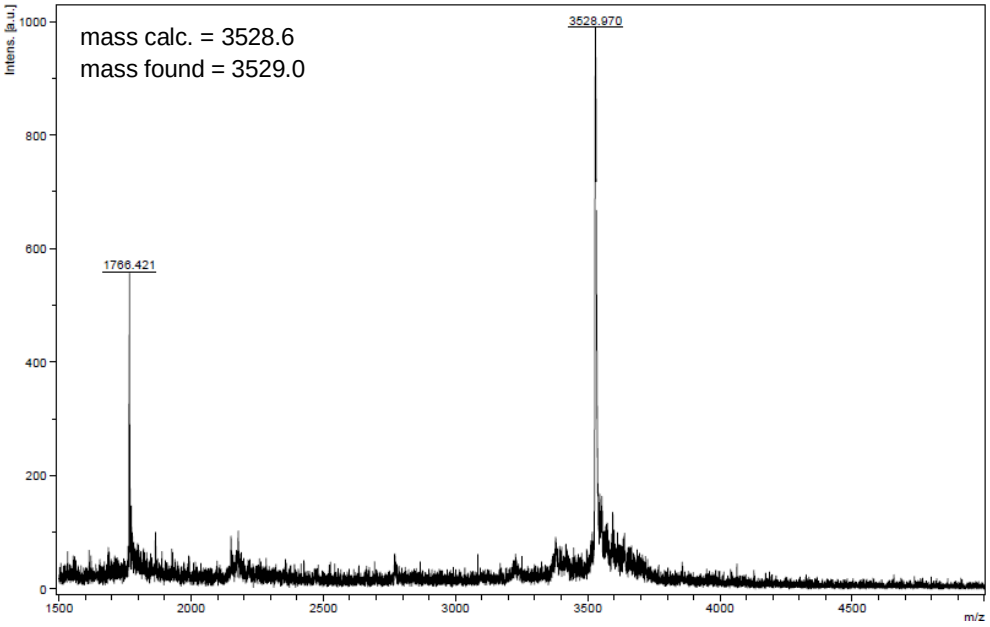
HPLC trace of isolated product 19j (Analytical RP-HPLC, Method-II)



Peak list:

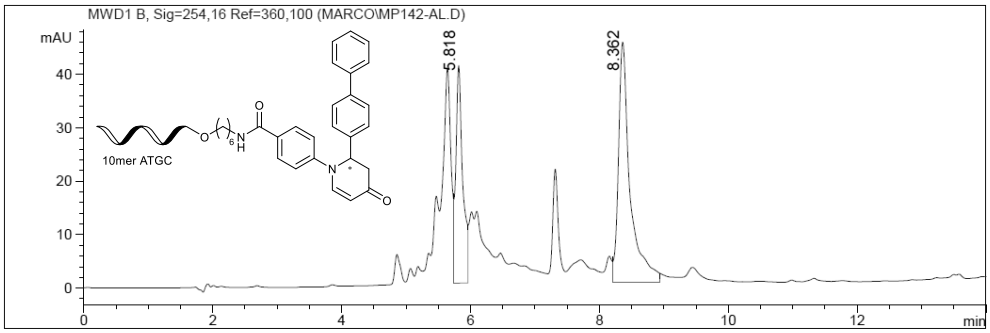
Ret. Time	Width min	Height	Area	Area %
8.629	0.210	38.134	480.948	100.000

MALDI-MS spectrum of isolated product 19j



DNA conjugate 19k: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 4-phenylbenzaldehyde **18k** and Danishefsky's diene **13** according to RP-08.

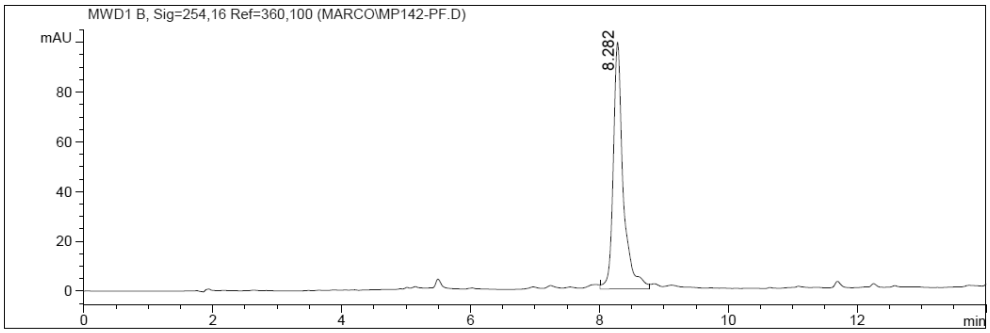
HPLC trace of crude reaction mixture 19k (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.818	0.125	40.785	305.138	35.237
8.362	0.208	44.986	560.832	64.763

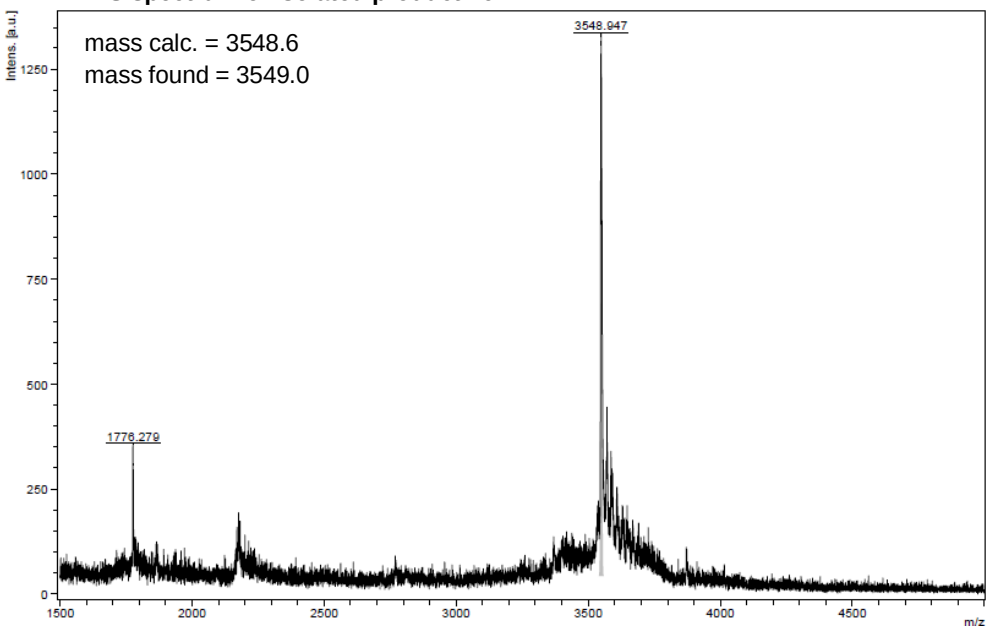
HPLC trace of isolated product 19k (Analytical RP-HPLC, Method-II)



Peak list:

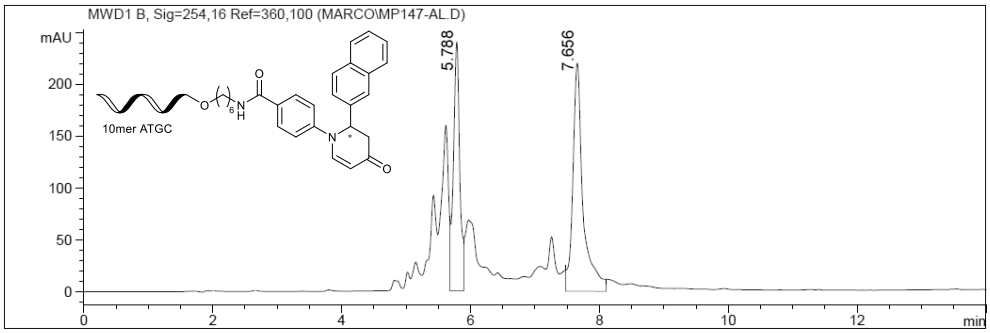
Ret. Time	Width min	Height	Area	Area %
8.282	0.156	99.102	1055.324	100.000

MALDI-MS spectrum of isolated product 19k



DNA conjugate 19l: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 2-Naphthaldehyde **18l** and Danishefsky's diene **13** according to RP-08.

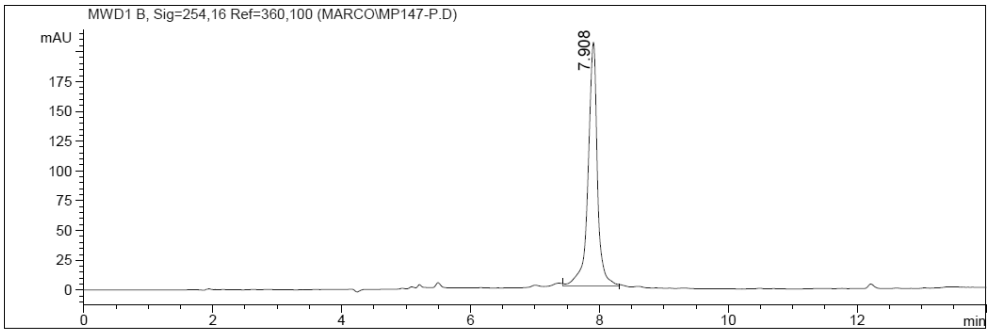
HPLC trace of crude reaction mixture 19l (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.788	0.113	240.849	1630.942	40.280
7.656	0.183	220.402	2418.100	59.720

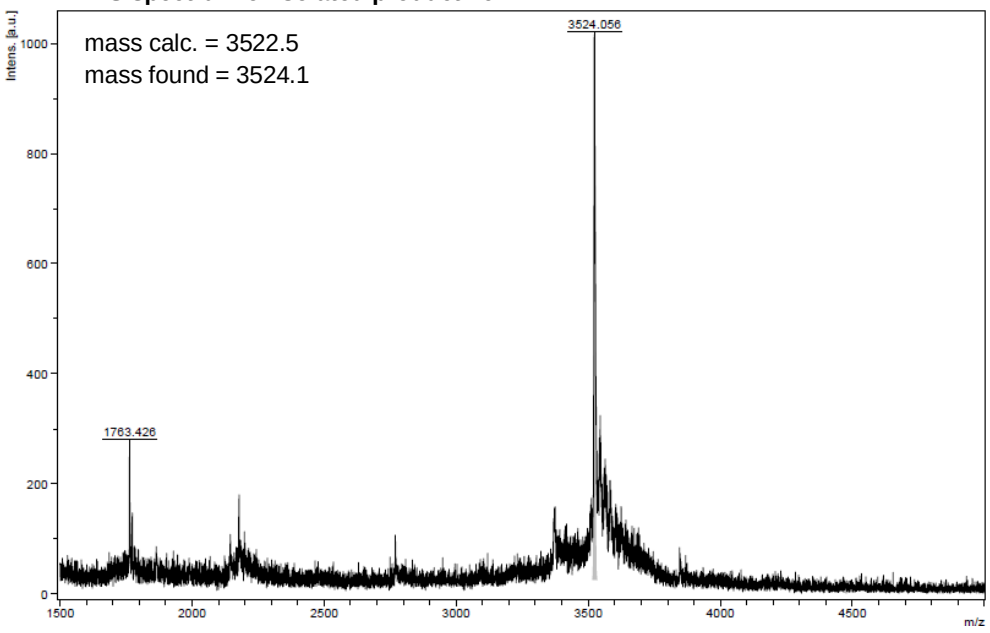
HPLC trace of isolated product 19l (Analytical RP-HPLC, Method-II)



Peak list:

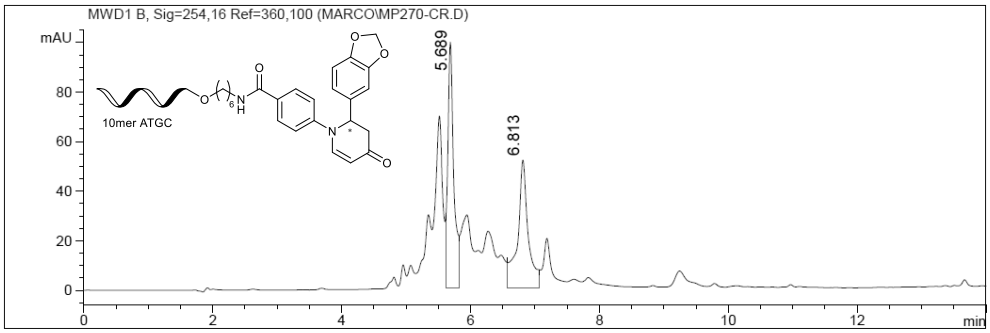
Ret. Time	Width min	Height	Area	Area %
7.908	0.167	204.996	2055.109	100.000

MALDI-MS spectrum of isolated product 19l



DNA conjugate 19m: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with piperonyl aldehyde **18m** and Danishefsky's diene **13** according to RP-08.

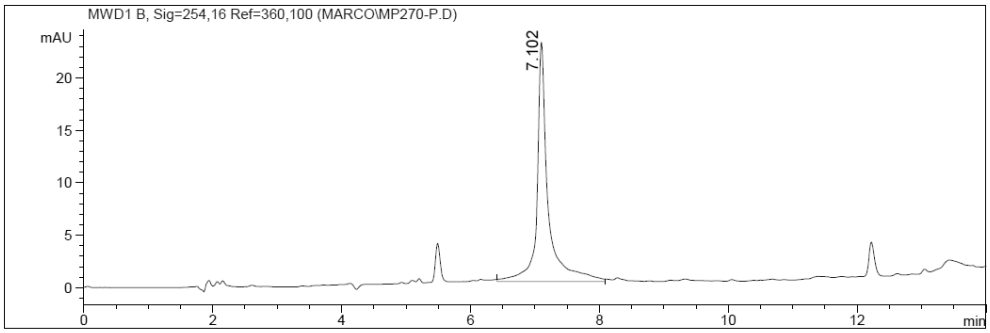
HPLC trace of crude reaction mixture 19m (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.689	0.107	99.124	638.691	52.502
6.813	0.187	51.512	577.815	47.498

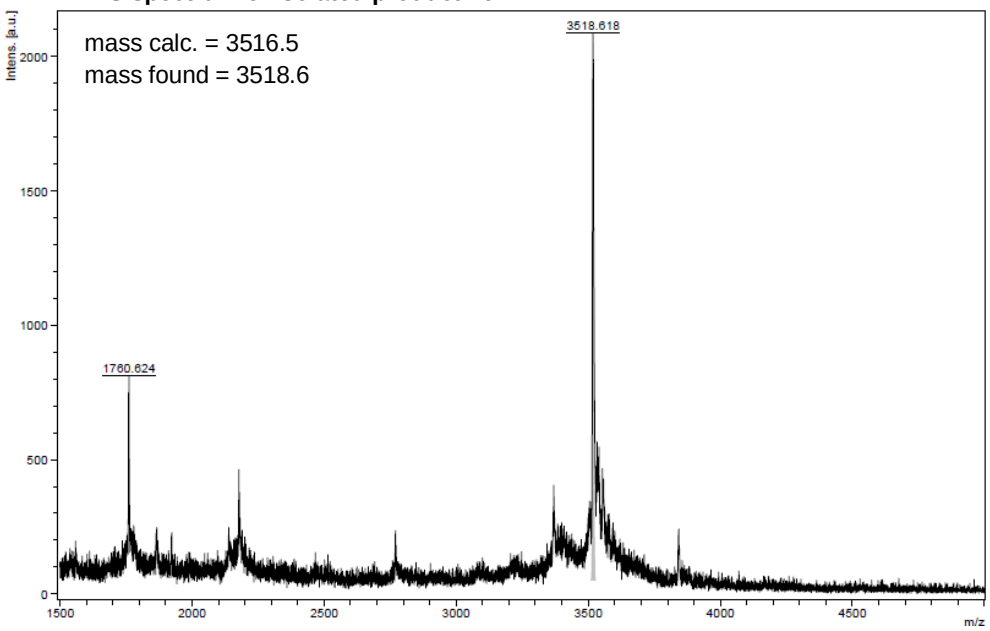
HPLC trace of isolated product 19m (Analytical RP-HPLC, Method-II)



Peak list:

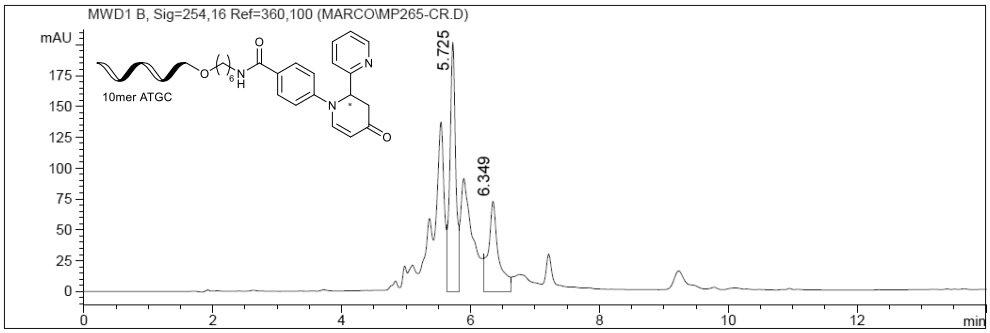
Ret. Time	Width min	Height	Area	Area %
7.102	0.163	22.801	272.139	100.000

MALDI-MS spectrum of isolated product 19m



DNA conjugate 19n: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 2-pyridinecarbox-aldehyde **18n** and Danishefsky's diene **13** according to RP-08.

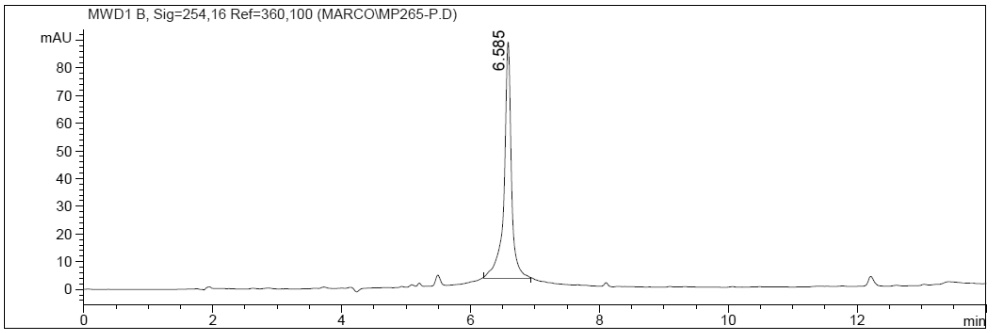
HPLC trace of crude reaction mixture 19n (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.725	0.106	202.771	1295.430	61.531
6.349	0.183	73.610	809.890	38.469

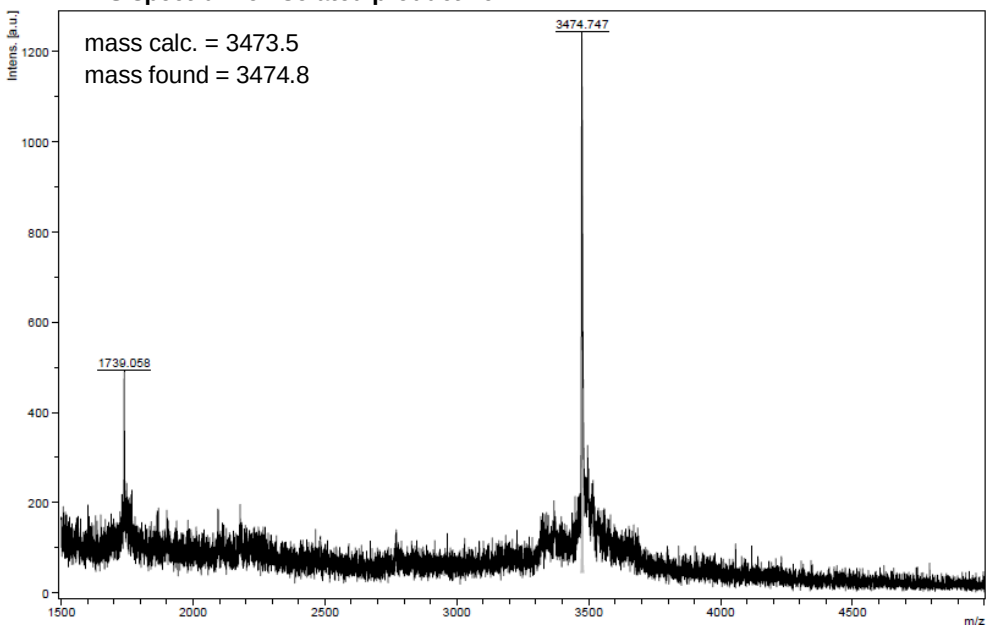
HPLC trace of isolated product 19n (Analytical RP-HPLC, Method-II)



Peak list:

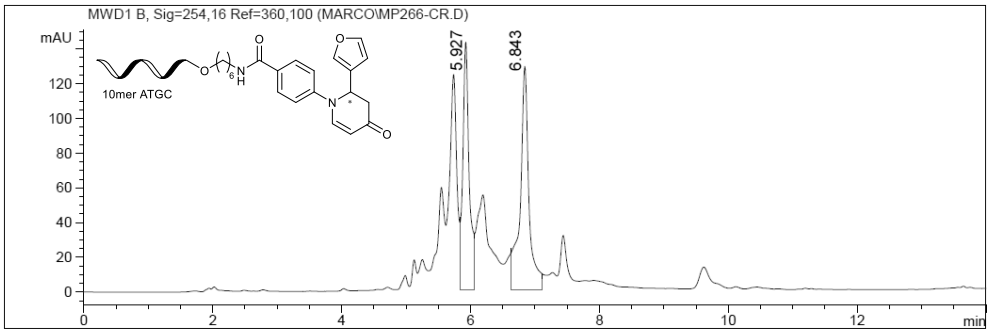
Ret. Time	Width min	Height	Area	Area %
6.585	0.133	85.834	684.034	100.000

MALDI-MS spectrum of isolated product 19n



DNA conjugate 19o: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with 3-furancarboxaldehyde **18o** and Danishefsky's diene **13** according to RP-08.

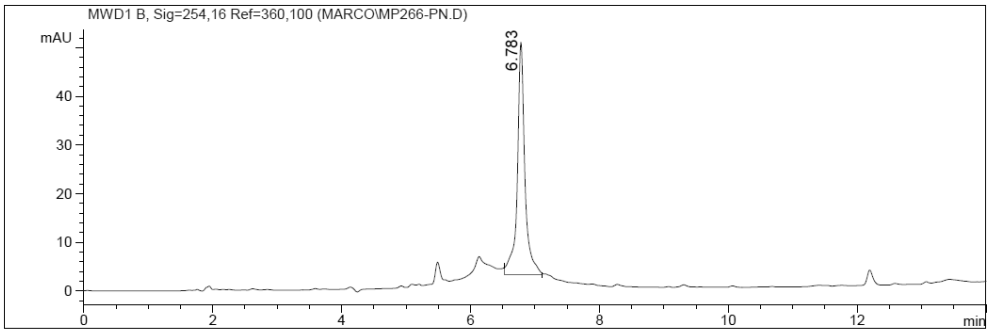
HPLC trace of crude reaction mixture 19o (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.927	0.113	143.131	972.186	44.381
6.843	0.157	129.107	1218.370	55.619

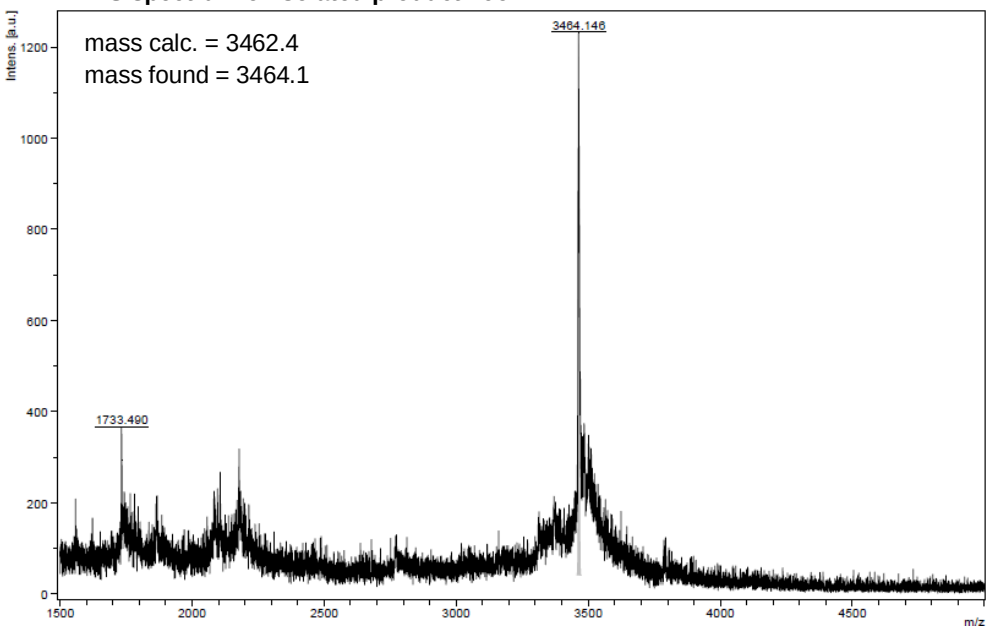
HPLC trace of isolated product 19o (Analytical RP-HPLC, Method-II)



Peak list:

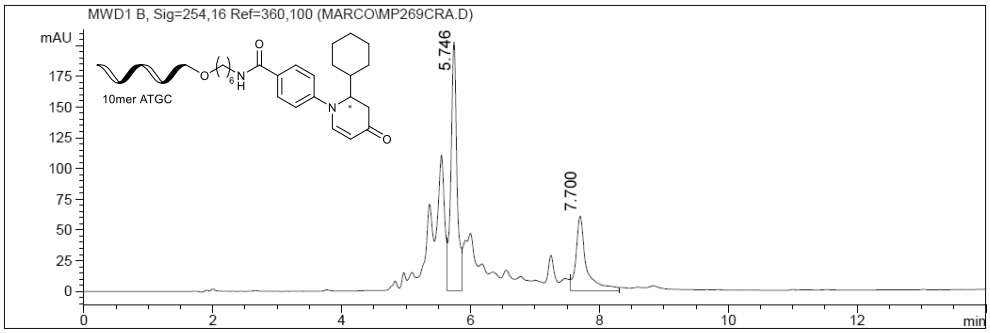
Ret. Time	Width min	Height	Area	Area %
6.783	0.137	47.909	392.414	100.000

MALDI-MS spectrum of isolated product 19o



DNA conjugate 19p: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with cyclohexanecarbox-aldehyde **18p** and Danishefsky's diene **13** according to RP-08.

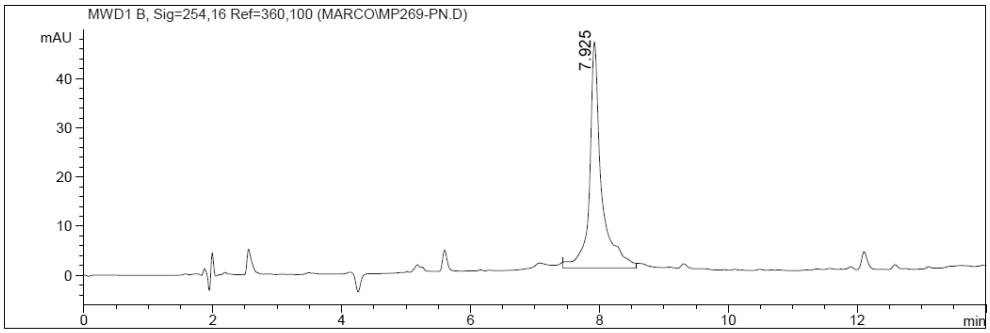
HPLC trace of crude reaction mixture 19p (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.746	0.109	203.173	1326.133	65.765
7.700	0.189	60.841	690.349	34.235

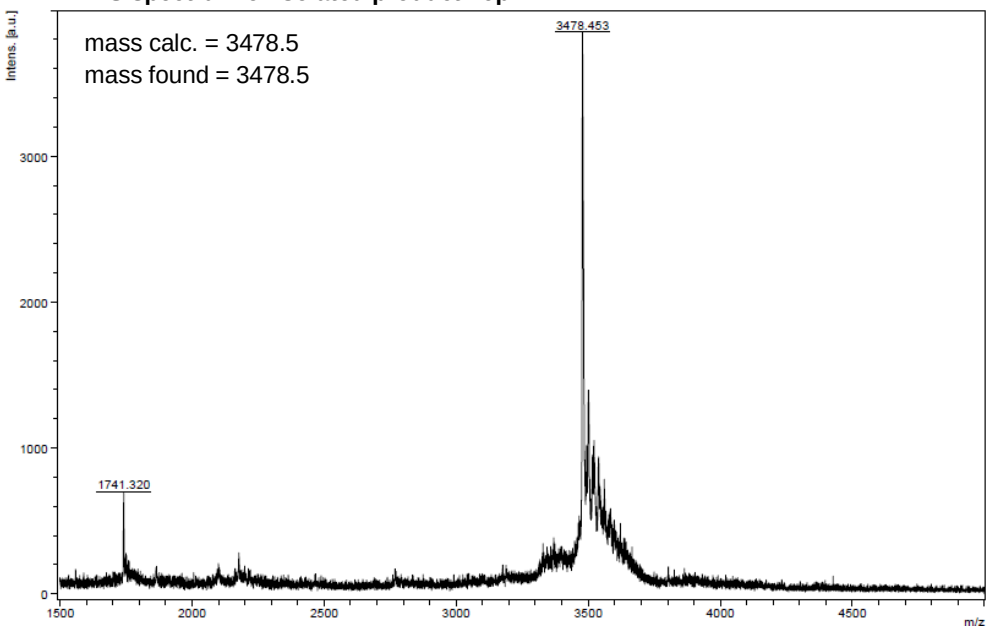
HPLC trace of isolated product 19p (Analytical RP-HPLC, Method-II)



Peak list:

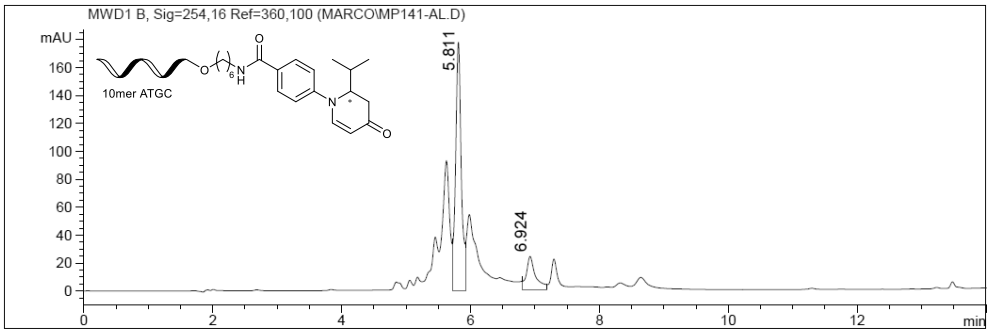
Ret. Time	Width min	Height	Area	Area %
7.925	0.213	46.069	590.128	100.000

MALDI-MS spectrum of isolated product 19p



DNA conjugate 19q: CPG-coupled 10mer ATGC-aniline conjugate **17** was reacted with isobutyraldehyde **18q** and Danishefsky's diene **13** according to RP-08.

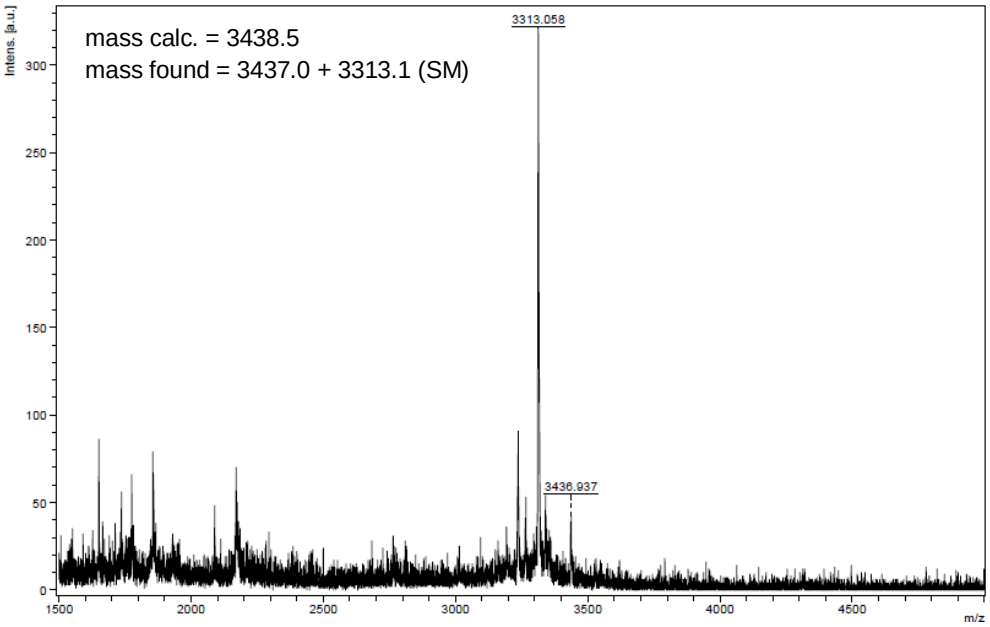
HPLC trace of crude reaction mixture 19q (Analytical RP-HPLC, Method-II)



Peak list:

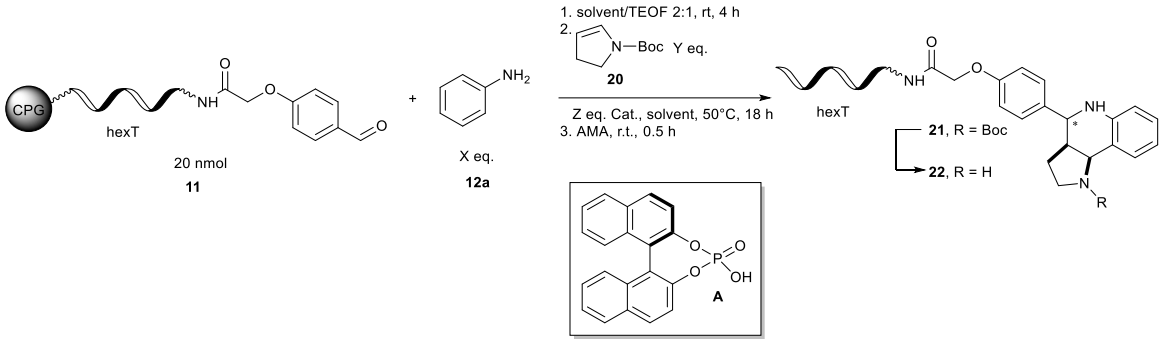
Ret. Time	Width min	Height	Area	Area %
5.811	0.102	178.303	1095.891	81.668
6.924	0.169	24.237	245.991	18.332

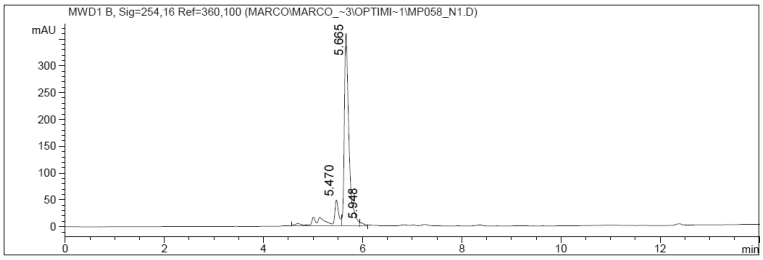
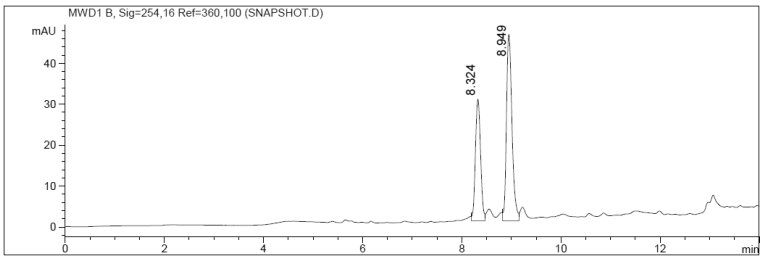
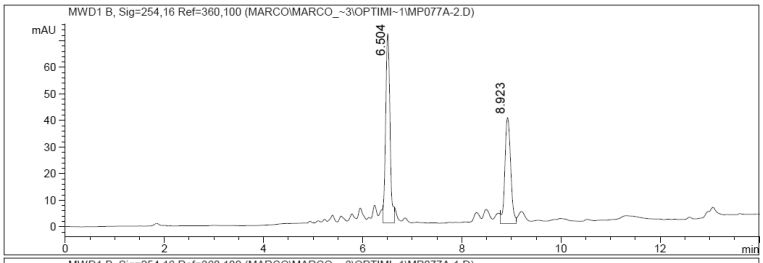
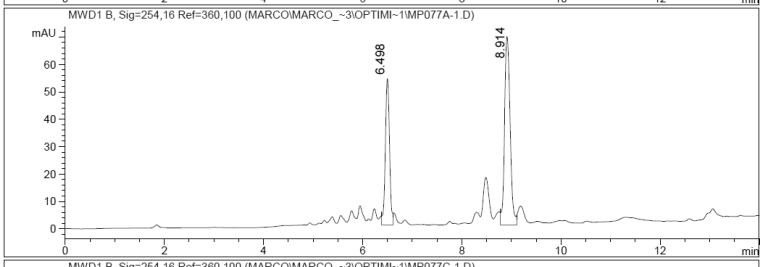
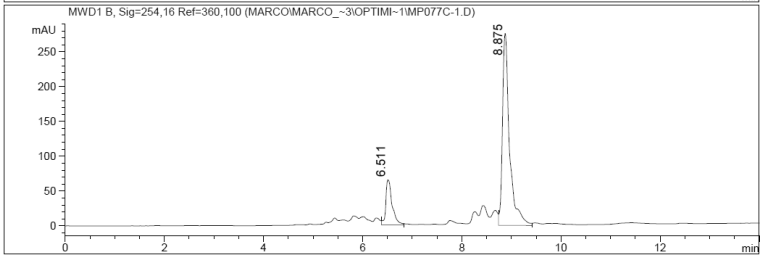
MALDI-MS spectrum of isolated product 19q



(*R*)-(-)-BNDHP-mediated Povarov reaction on CPG-coupled oligonucleotides

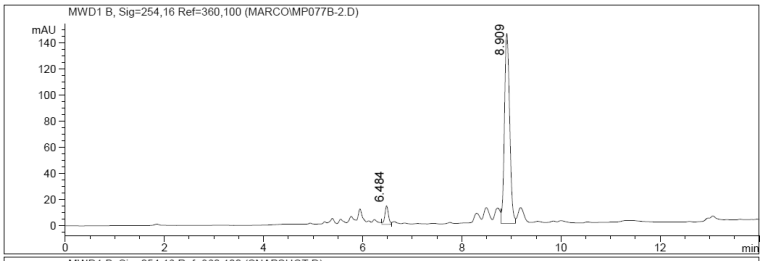
Table S9 Optimization of *(R)*-(-)-BNDHP-mediated Povarov reaction CPG-coupled hexT-aldehyde conjugate.[a]



Entry	Reaction conditions[b]	HPLC trace of crude reaction mixture[c]
1	hexT-aldehyde conjugate **11**	
2	hexT-tetrahydroquinoline conjugate **21**	
3	1. 500 equiv. **12a** CH_2Cl_2/TEOF (2:1), 4 h, rt 2. 500 equiv. **20** 50 equiv. ***Yb(OTf)$_3$*** CH_2Cl_2, 18 h, rt => conversion 42 %	
4	1. 500 equiv. **12a** THF/TEOF (2:1), 4 h, rt 2. 500 equiv. **20** 50 equiv. ***Yb(OTf)$_3$*** THF, 18 h, 50 °C => conversion 63 %	
5	1. 500 equiv. **12a** THF/TEOF (2:1), 4 h, rt 2. 500 equiv. **20** ***50 equiv*. *(R)-(-)-BNDHP* A** THF, 18 h, 50 °C => conversion 82 %	

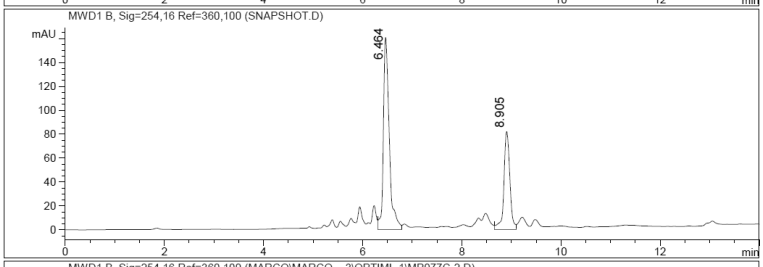
6 1. 500 equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **20**
100 equiv. (*R*)-(-)-BNDHP **A**
THF, 18 h, 50 °C

=> conversion 94 %



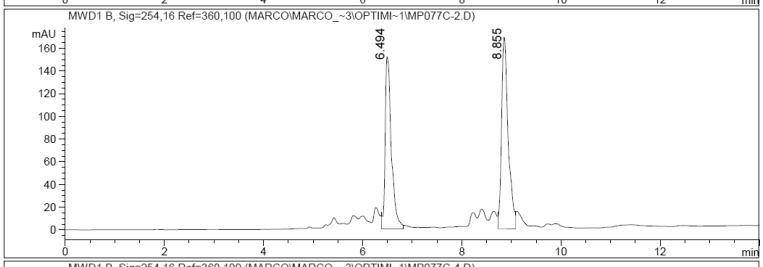
7 1. 500 equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **20**
THF, 18 h, 50 °C

=> conversion 34 %



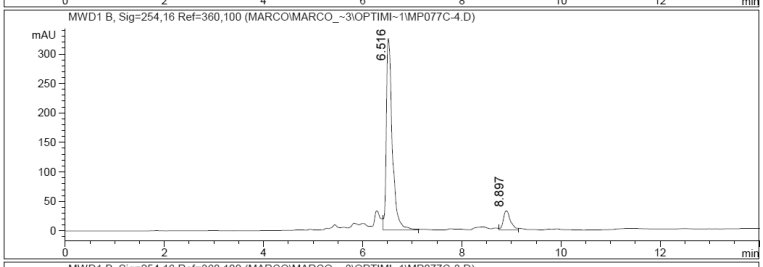
8 1. ***1000*** equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **20**
50 equiv. (*R*)-(-)-BNDHP **A**
THF, 18 h, 50 °C

=> conversion 55 %



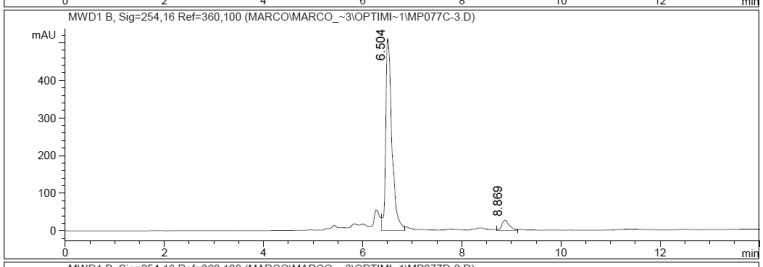
9 1. ***2000*** equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **20**
50 equiv. (*R*)-(-)-BNDHP **A**
THF, 18 h, 50 °C

=> conversion 11 %



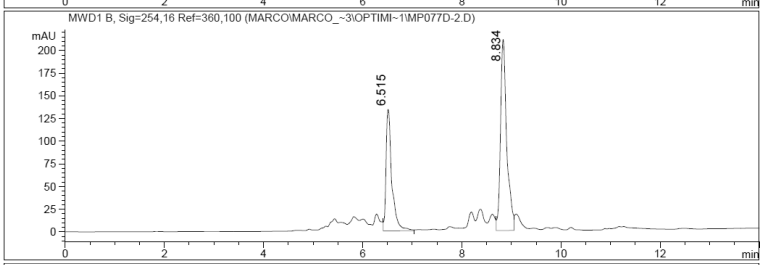
10 1. ***4000*** equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. 500 equiv. **20**
50 equiv. (*R*)-(-)-BNDHP **A**
THF, 18 h, 50 °C

=> conversion 7 %



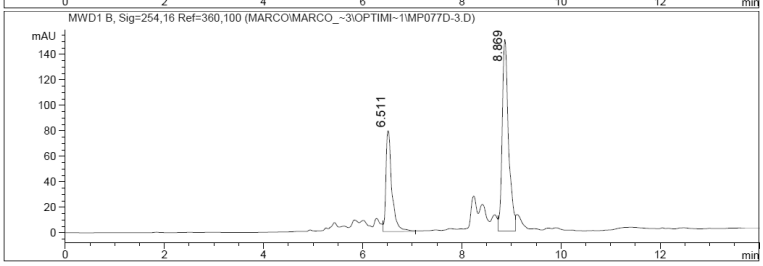
11 1. 500 equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. ***1000*** equiv. **20**
50 equiv. (*R*)-(-)-BNDHP **A**
THF, 18 h, 50 °C

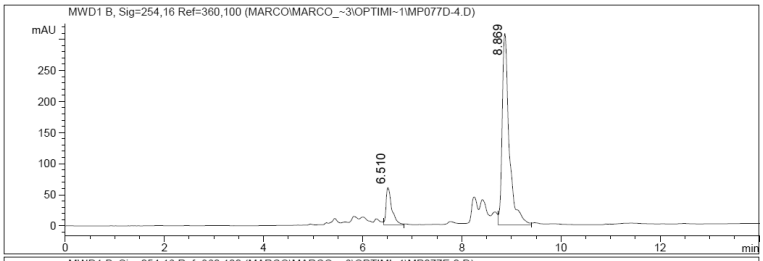
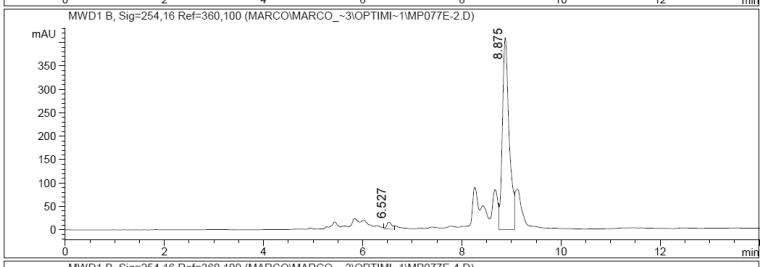
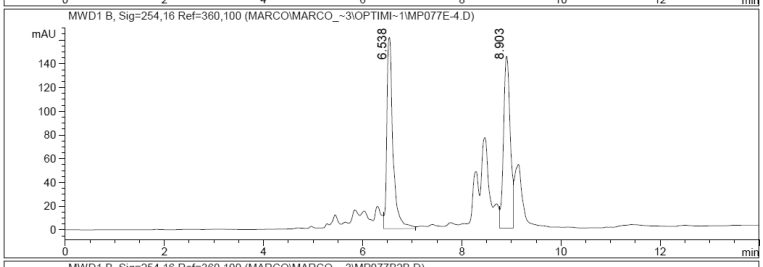
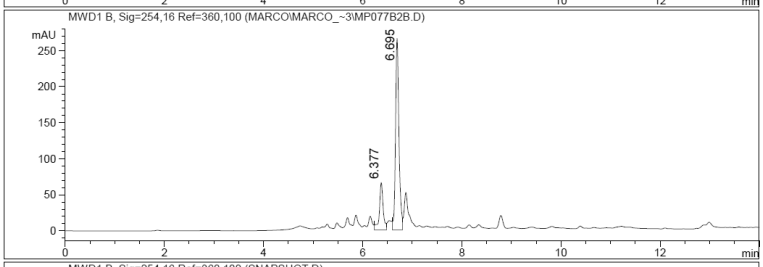
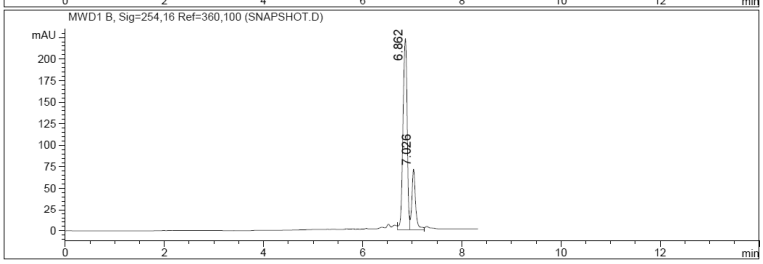
=> conversion 63 %



12 1. 500 equiv. **12a**
THF/TEOF (2:1), 4 h, rt
2. ***2000*** equiv. **20**
50 equiv. (*R*)-(-)-BNDHP **A**
THF, 18 h, 50 °C

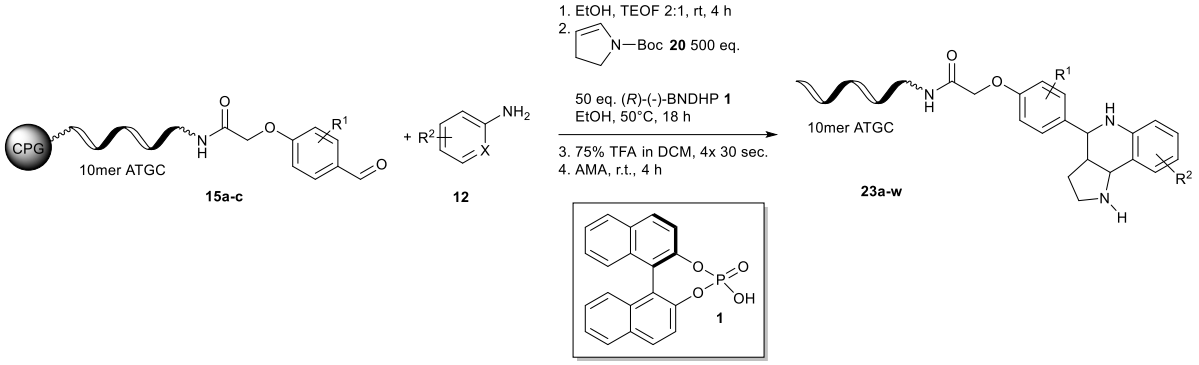
=> conversion 67 %



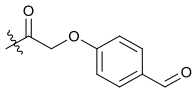
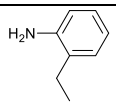
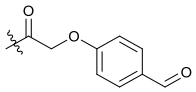
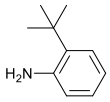
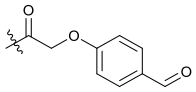
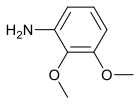
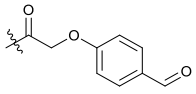
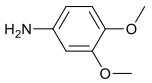
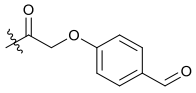
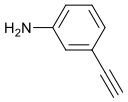
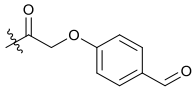
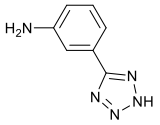
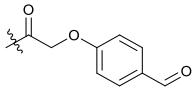
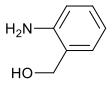
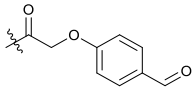
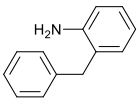
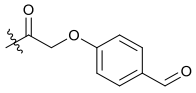
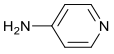
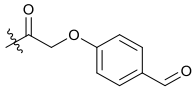
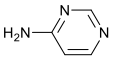
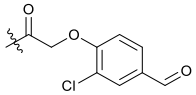
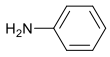
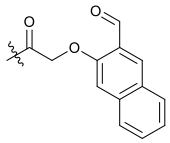
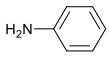
13	1. 500 equiv. **12a** THF/TEOF (2:1), 4 h, rt 2. ***4000*** equiv. **20** 50 equiv. (*R*)-(-)-BNDHP **A** THF, 18 h, 50 °C => conversion 86 %	
14	1. 500 equiv. **12a** ***EtOH***/TEOF (2:1), 4 h, rt 2. 500 equiv. **20** 50 equiv. (*R*)-(-)-BNDHP **A** ***EtOH***, 18 h, 50 °C => conversion > 95 %	
15	1. 500 equiv. 12a ***DMF***/TEOF (2:1), 4 h, rt 2. 500 equiv. 20 50 equiv. (*R*)-(-)-BNDHP **A** ***DMF***, 18 h, 50 °C => conversion 50 %	
17	1. 500 equiv. **12a** THF/TEOF (2:1), 4 h, rt 2. 500 equiv. **20** 50 equiv. (*R*)-(-)-BNDHP **A** THF, 18 h, 50 °C 3. 10% TFA, 4 h, rt => conversion 82 %	
18	hexT-tetrahydroquinoline conjugate **22**	

[a] Condensation of CPG-coupled hexT conjugate **11a** (20 nmol) with aniline **12a** (X equiv.) in 36 µL of indicated solvent/triethyl orthoformate (2:1) at ambient temperature for 4 h, then (*R*)-(-)-BNDHP **A** (X equiv.) dissolved in 30 µL of indicated solvent and *N*-Boc-2,3-dihydro-1H-pyrrole **20** (X equiv.) were added, the reaction mixture was shaken at indicated temperature for 16 h. [b] parameters that were changed are in bold and italic. [c] Analytical RP-HPLC, Method-III. TEOF = triethyl orthoformate.

Table S10 – Scope of (*R*)-(-)-BNDHP-mediated Povarov reaction on CPG-coupled 10mer ATGC oligonucleotide-aldehyde conjugate.[a]



Entry	Product	DNA-aldehyde conjugate	Amine	Conversion [%][b]	Mass$_{calc.}$ Mass$_{found}$[c]
1	**23a**	**15a**	**12a**	91	3503.5 3502.8
2	**23b**	**15a**	**12i**	57	3582.4 3583.4
3	**23c**	**15a**	**12h**	> 95	3582.4 3582.3
4	**23d**	**15a**	**12e**	84	3521.5 3522.6 (Dia1) 3522.9 (Dia2)
5	**23e**	**15a**	**12f**	90	3521.5 3522.8
6	**23f**	**15a**	**12g**	86	3539.5 3540.7
7	**23g**	**15a**	**12s**	83	3571.5 3572.8
8	**23h**	**15a**	**12t**	70	3547.6 3548.2
9	**23i**	**15a**	**12u**	58	3519.5 3518.6
10	**23j**	**15a**	**12b**	87	3531.6 3531.6
11	**23k**	**15a**	**12c**	92	3531.6 3533.0

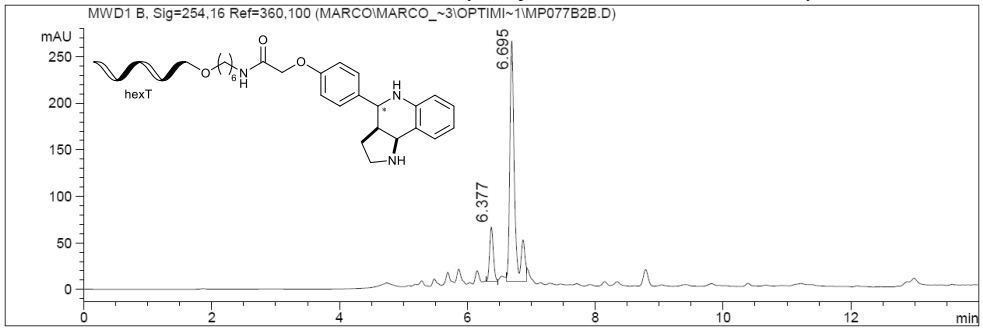
12	**23l**	 **15a**	 **12d**	39	3531.6 3532.7
13	**23m**	 **15a**	 **12k**	< 5	3559.7 n.d.
14	**23n**	 **15a**	 **12m**	82	3563.6 3564.5
15	**23o**	 **15a**	 **12l**	86	3563.6 3561.7
16	**23p**	 **15a**	 **12o**	94	3527.6 3527.9
17	**23q**	 **15a**	 **12p**	>95	3571.6 3573.3
18	**23r**	 **15a**	 **12v**	75	3533.6 3534.3
19	**23s**	 **15a**	 **12w**	25	3593.7 3591.4
20	**23t**	 **15a**	 **12q**	< 5	3504.5 n.d.
21	**23u**	 **15a**	 **12x**	< 5	3505.5 n.d.
22	**23v**	 **15b**	 **12a**	93	3538.0 3537.6
23	**23w**	 **15c**	 **12a**	< 5	3553.6 n.d.

[a] Condensation of CPG-coupled oligonucleotide conjugate **15** (20 nmol) with aniline **12** (500 equiv., 10 µmol) in 36 µL ethanol/triethyl orthoformate (2:1) at ambient temperature for 4 h, then addition of (*R*)-(-)-BNDHP **A** (50 equiv., 1 µmol) dissolved in 30 µL ethanol and *N*-Boc-2,3-dihydro-1H-pyrrole **20** (500 equiv., 10 µmol) at 50 °C for 16 h. 75% TFA in dichloromethane 4x 30 seconds at ambient temperature. DNA cleavage AMA (30 % aqueous ammonia / 40 % aqueous methylamine, 1:1 (vol/vol)) at ambient temperature for 4 h. [b] Determined by analytical RP-HPLC analysis. [c] Measured by MALDI-MS. 10mer ATGC = 5'-GTC ATG ATC T-3'. n.d. = not detected.

Products of Povarov reaction on CPG-coupled oligonucleotide-aldehyde conjugate

DNA conjugate 22: CPG-coupled hexT-aldehyde conjugate **11** was reacted with aniline **12a** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

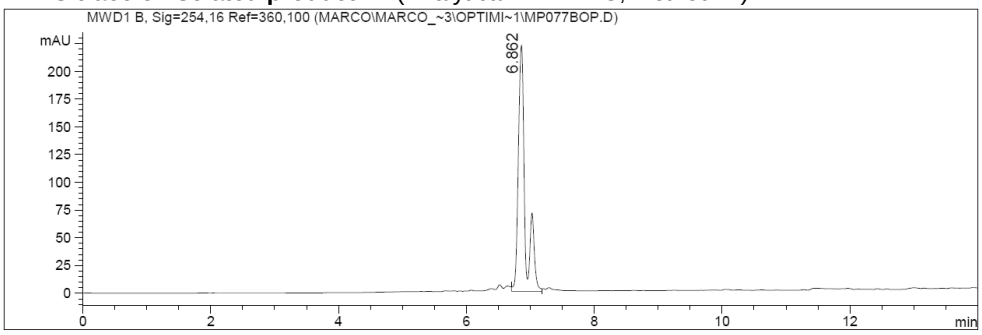
HPLC trace of crude reaction mixture 22 (Analytical RP-HPLC, Method-III)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.377	0.068	58.738	239.068	14.781
6.695	0.089	259.027	1378.315	85.219

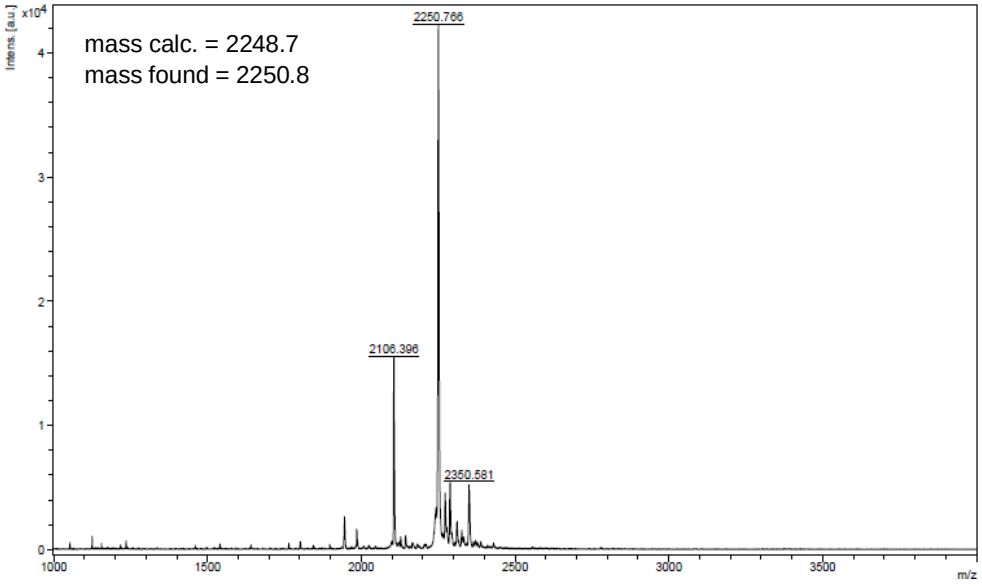
HPLC trace of isolated product 22 (Analytical RP-HPLC, Method-III)



Peak list:

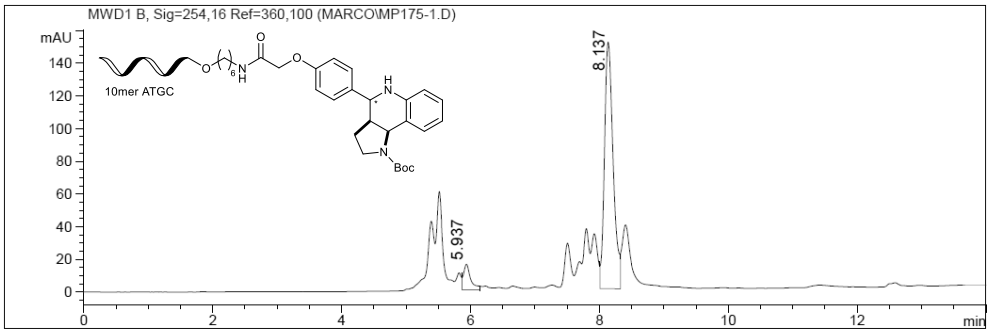
Ret. Time	Width min	Height	Area	Area %
6.862	0.123	222.063	1633.396	100.000

MALDI-MS spectrum of crude reaction mixture 22



DNA conjugate 23a: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with aniline **12a** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

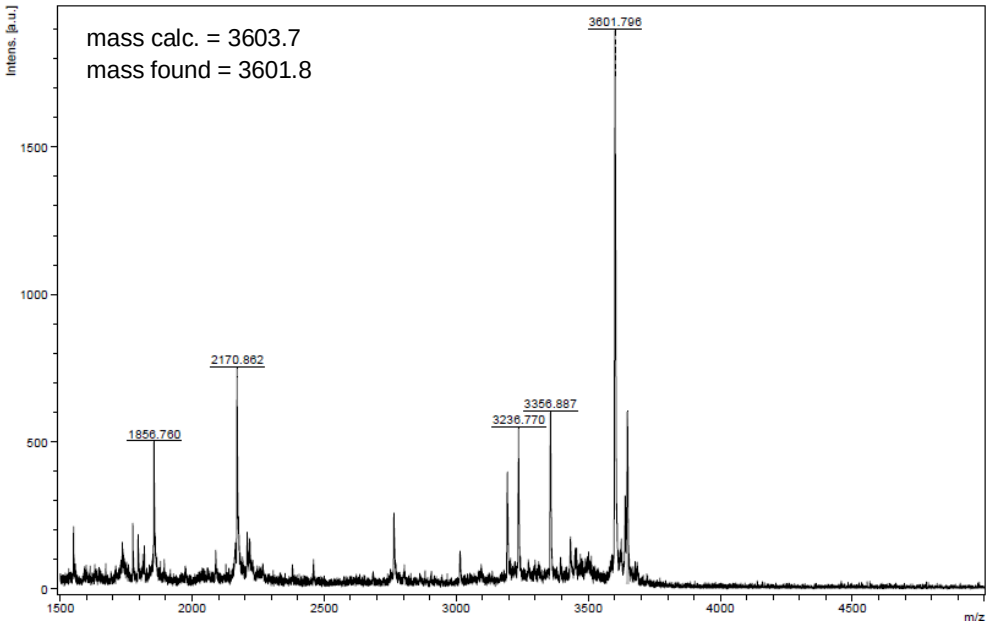
HPLC trace of crude reaction mixture 23a-Boc$_{on}$ (Analytical RP-HPLC, Method-II)



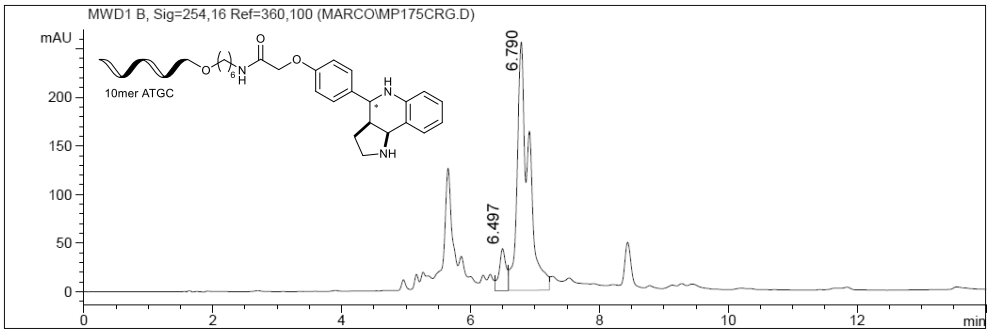
Peak list:

Ret. Time	Width min	Height	Area	Area %
5.937	0.127	15.722	119.679	7.863
8.137	0.155	150.913	1402.450	92.137

MALDI-MS spectrum of crude reaction mixture 23a-Boc$_{on}$



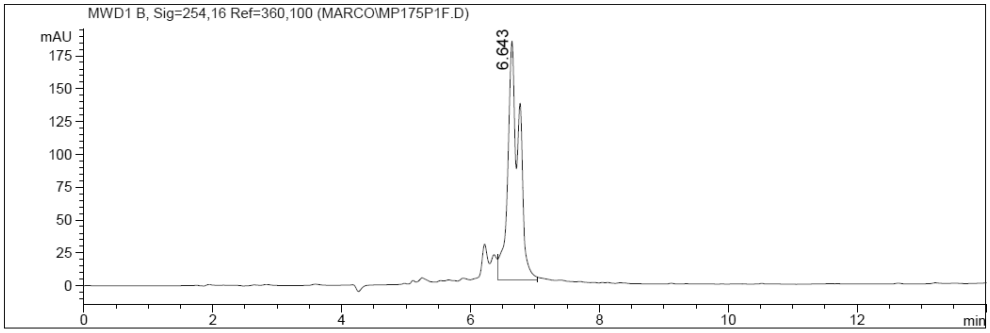
HPLC trace of crude reaction mixture 23a (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.497	0.125	43.055	321.970	9.172
6.790	0.208	255.855	3188.387	90.828

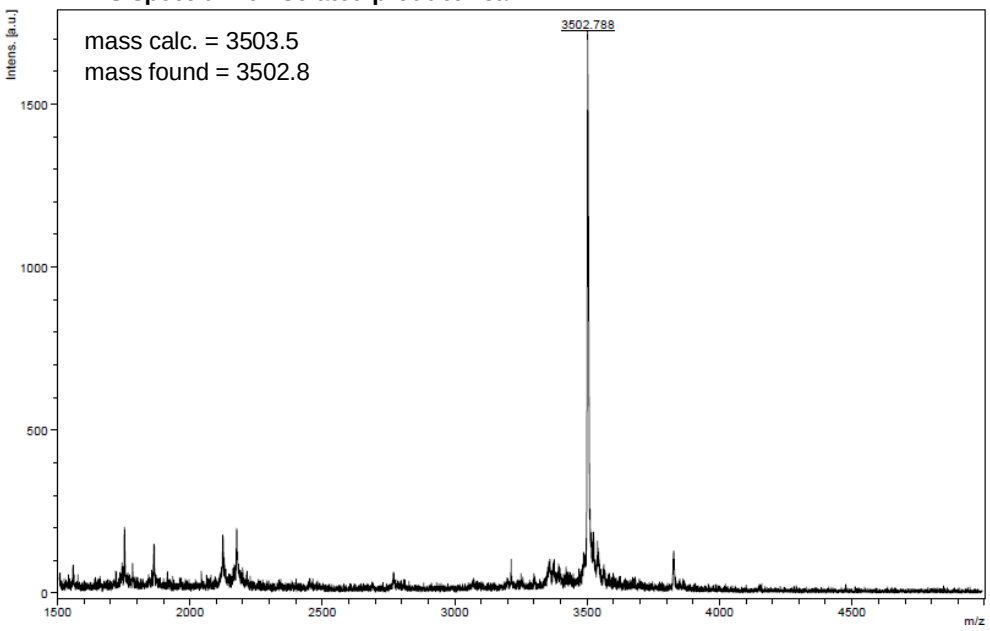
HPLC trace of isolated product 23a (Analytical RP-HPLC, Method-II)



Peak list:

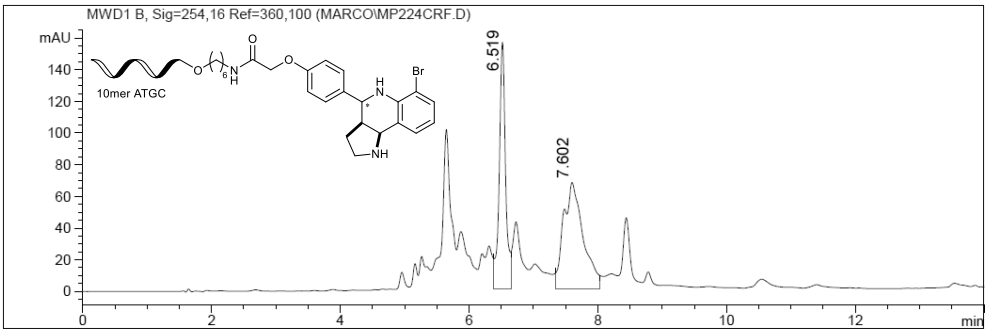
Ret. Time	Width min	Height	Area	Area %
6.643	0.204	182.113	2225.986	100.000

MALDI-MS spectrum of isolated product 23a



DNA conjugate 23b: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-bromoaniline **12i** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

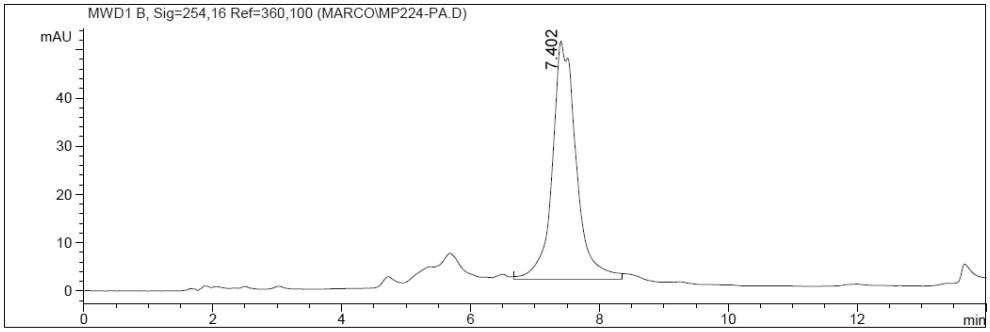
HPLC trace of crude reaction mixture 23b (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.519	0.112	155.924	1048.529	42.513
7.602	0.352	67.042	1417.842	57.487

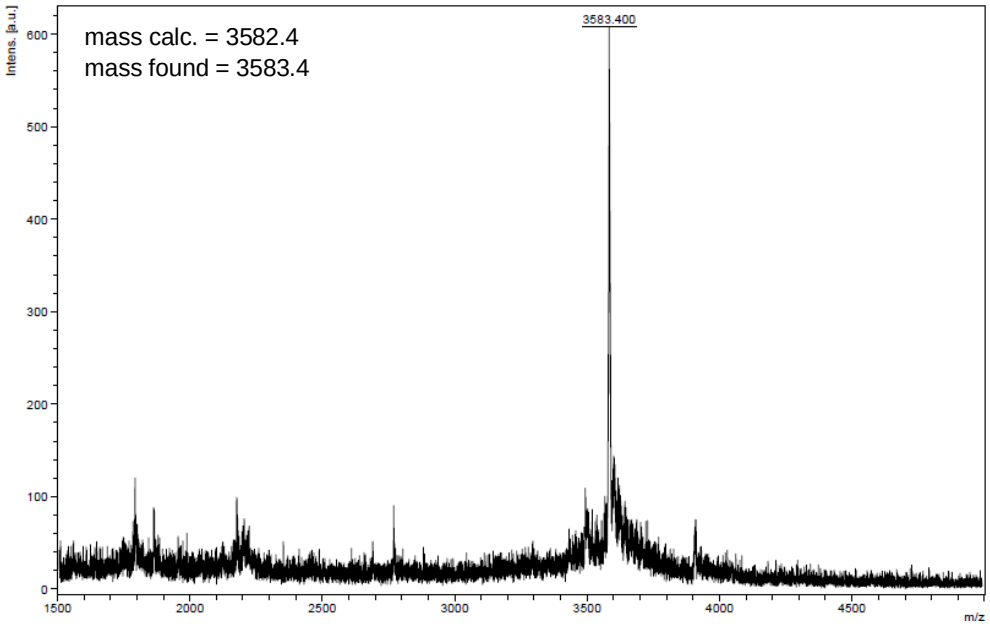
HPLC trace of isolated product 23b (Analytical RP-HPLC, Method-II)



Peak list:

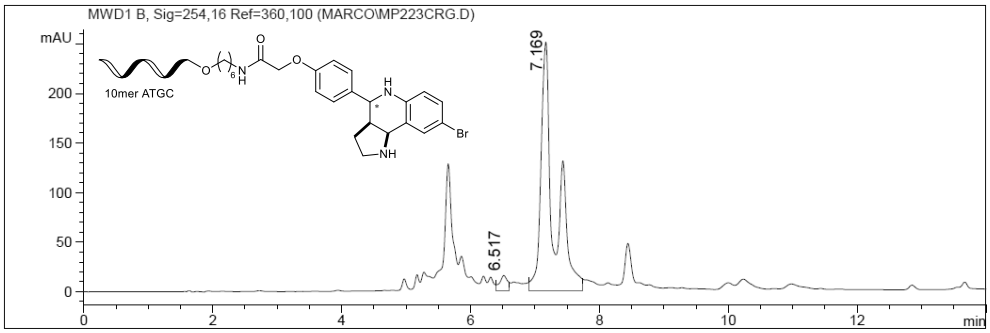
Ret. Time	Width min	Height	Area	Area %
7.402	0.431	49.421	1277.357	100.000

MALDI-MS spectrum of isolated product 23b



DNA conjugate 23c: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-bromoaniline **12h** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

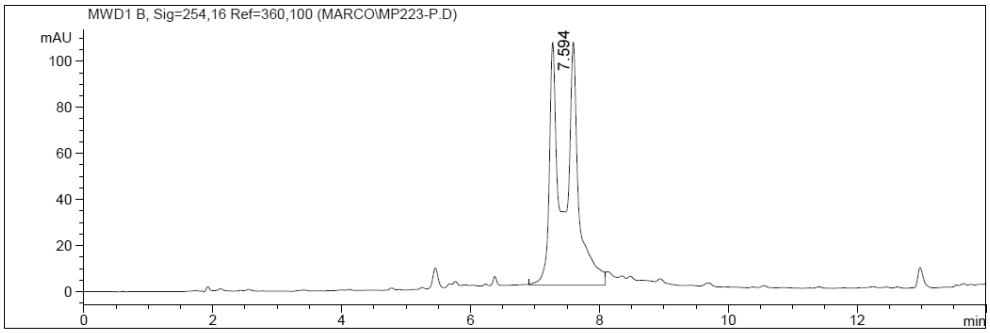
HPLC trace of crude reaction mixture 23c (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.517	0.135	14.963	120.802	3.374
7.169	0.230	250.566	3459.788	96.626

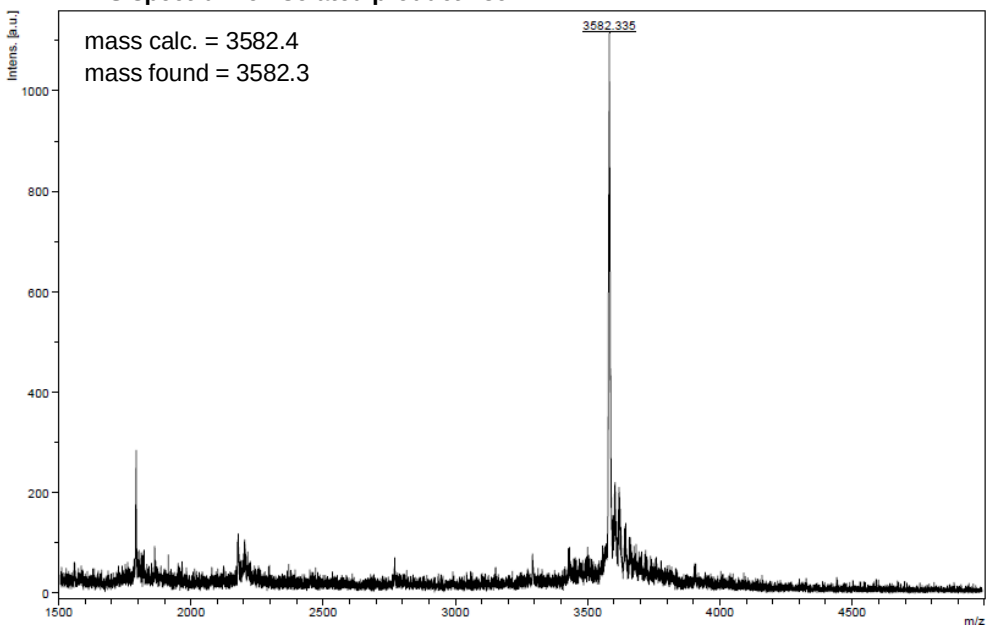
HPLC trace of isolated product 23c (Analytical RP-HPLC, Method-II)



Peak list:

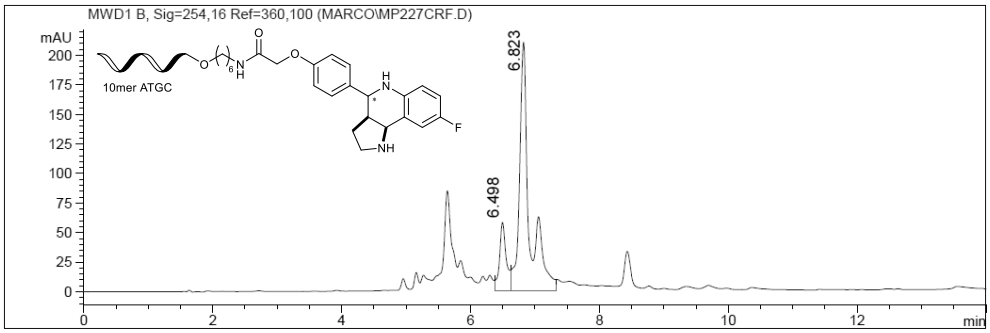
Ret. Time	Width min	Height	Area	Area %
7.594	0.326	105.461	2063.898	100.000

MALDI-MS spectrum of isolated product 23c



DNA conjugate 23d: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-fluoroaniline **12e** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

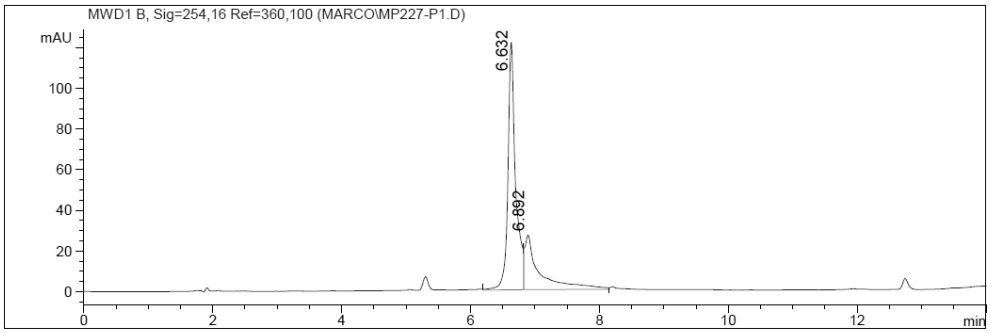
HPLC trace of crude reaction mixture 23d (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.498	0.121	58.176	424.096	15.997
6.823	0.176	210.615	2227.069	84.003

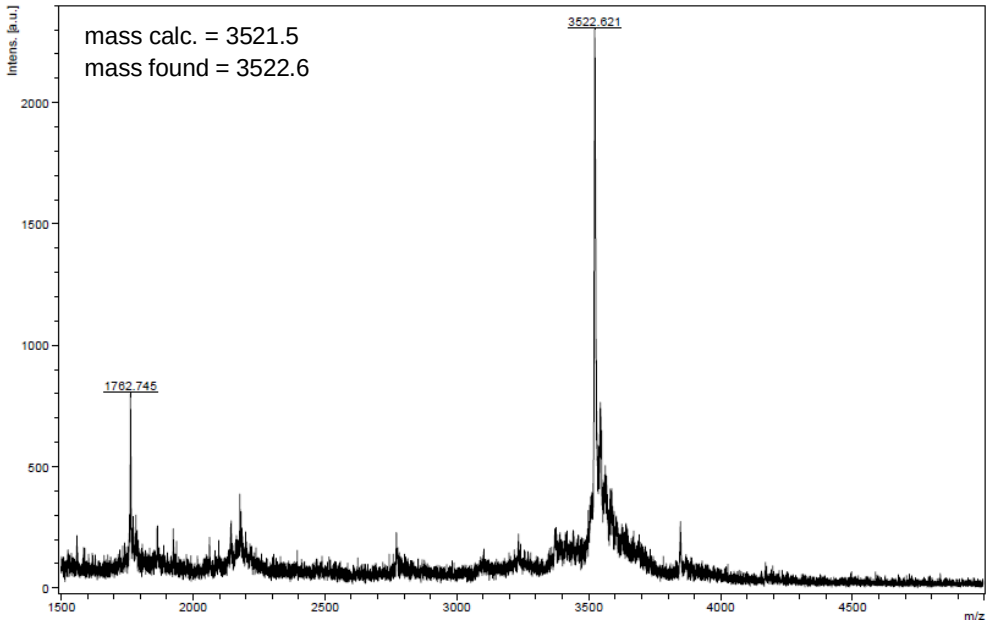
HPLC trace of isolated product 23d-dia1 (Analytical RP-HPLC, Method-II)



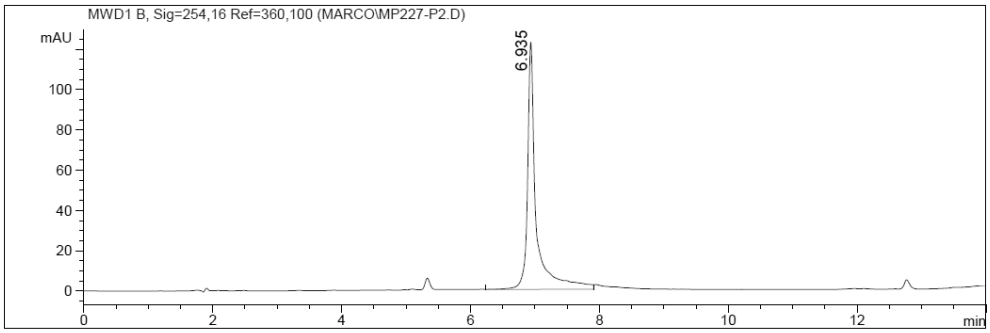
Peak list:

Ret. Time	Width min	Height	Area	Area %
6.632	0.117	121.831	1014.094	69.760
6.892	0.211	26.848	439.587	30.240

MALDI-MS spectrum of isolated product 23d-dia1



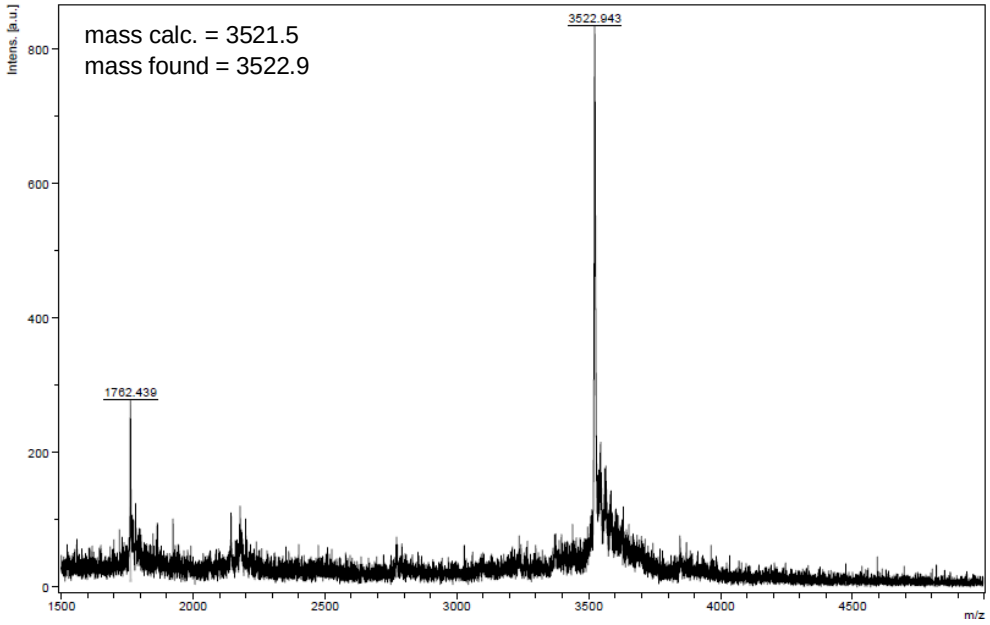
HPLC trace of isolated product 23d-dia2 (Analytical RP-HPLC, Method-II)



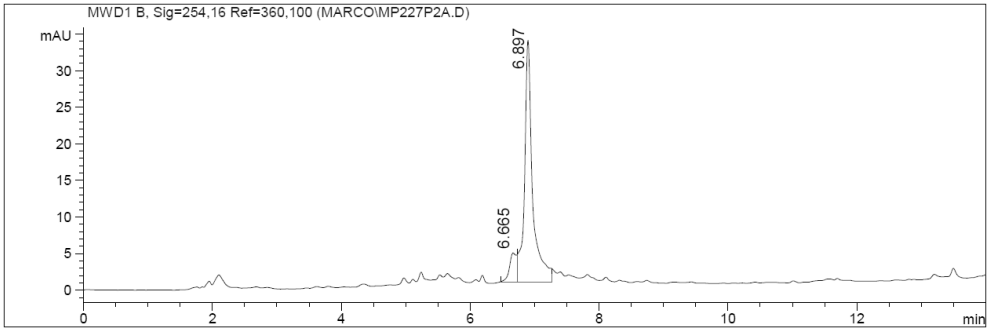
Peak list:

Ret. Time	Width min	Height	Area	Area %
6.935	0.130	122.672	1140.619	100.000

MALDI-MS spectrum of isolated product 23d-dia2



HPLC trace of isolated product 23d-dia2 after treatment with AMA (Analytical RP-HPLC, Method-II)

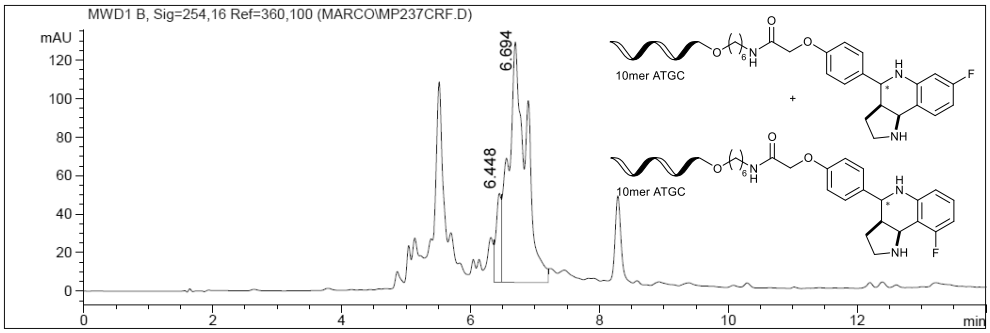


Peak list:

Ret. Time	Width min	Height	Area	Area %
6.665	0.138	3.993	32.941	10.336
6.897	0.144	33.125	285.757	89.664

DNA conjugate 23e: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-fluoroaniline **12f** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

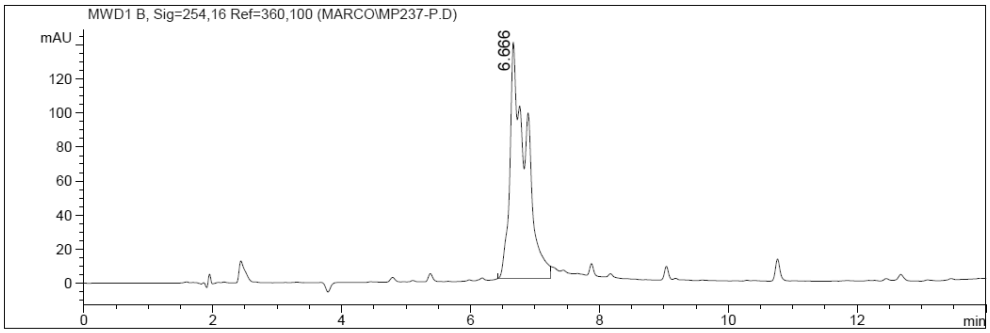
HPLC trace of crude reaction mixture 23e (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.448	0.094	46.279	260.954	9.840
6.694	0.319	125.116	2391.062	90.160

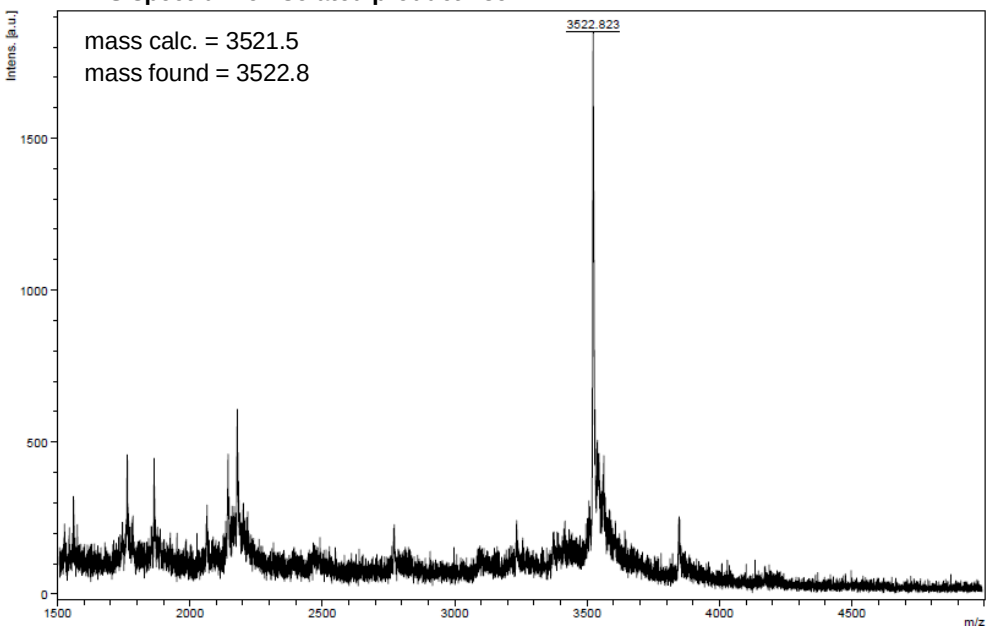
HPLC trace of isolated product 23e (Analytical RP-HPLC, Method-II)



Peak list:

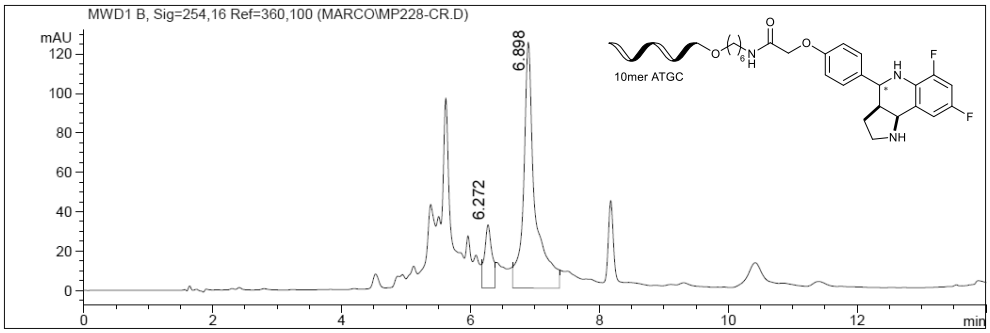
Ret. Time	Width min	Height	Area	Area %
6.666	0.289	138.906	2411.832	100.000

MALDI-MS spectrum of isolated product 23e



DNA conjugate 23f: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2,4-difluoroaniline **12g** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

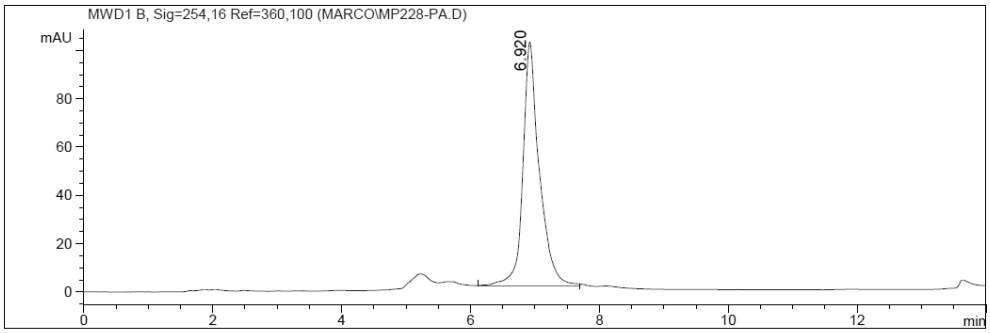
HPLC trace of crude reaction mixture 23f (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.272	0.134	32.186	259.067	14.481
6.898	0.204	124.958	1529.998	85.519

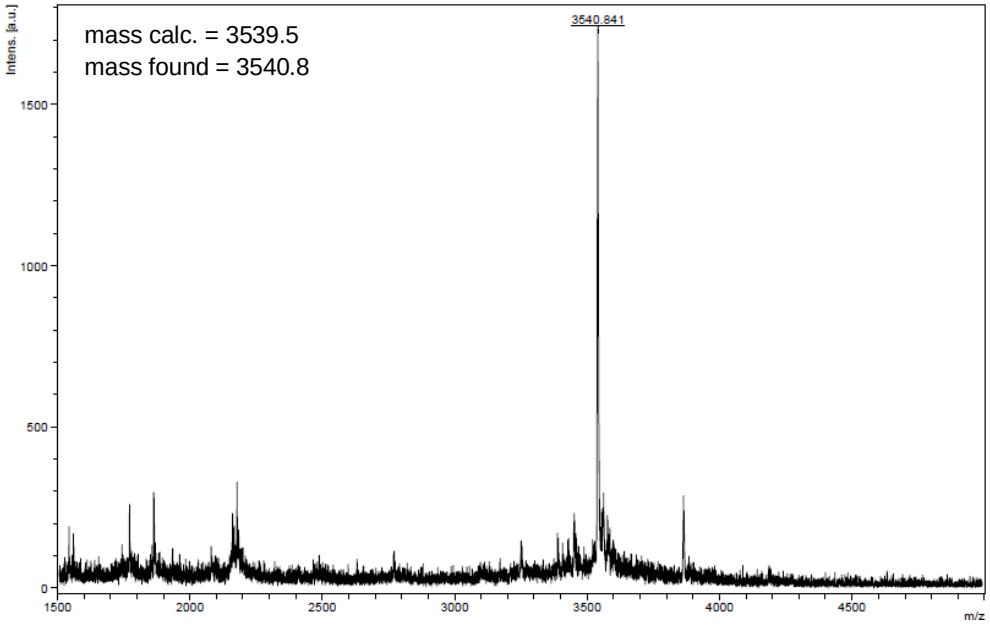
HPLC trace of isolated product 23f (Analytical RP-HPLC, Method-II)



Peak list:

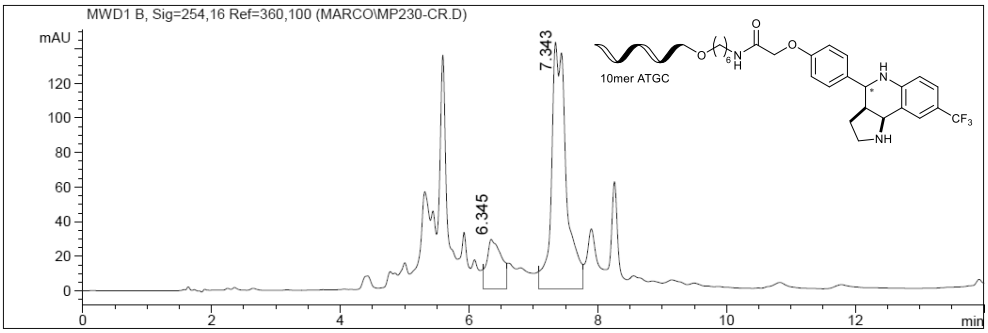
Ret. Time	Width min	Height	Area	Area %
6.920	0.295	100.973	1786.442	100.000

MALDI-MS spectrum of isolated product 23f



DNA conjugate 23g: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-trifluoromethylaniline **12s** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

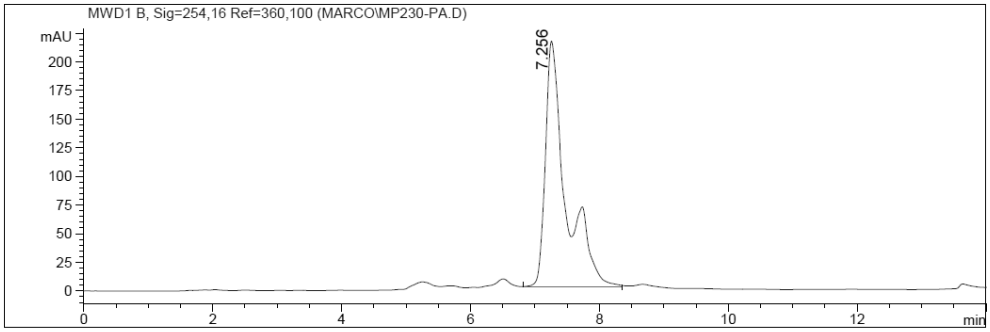
HPLC trace of crude reaction mixture 23g (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.345	0.264	28.950	458.510	16.627
7.343	0.268	143.194	2299.069	83.373

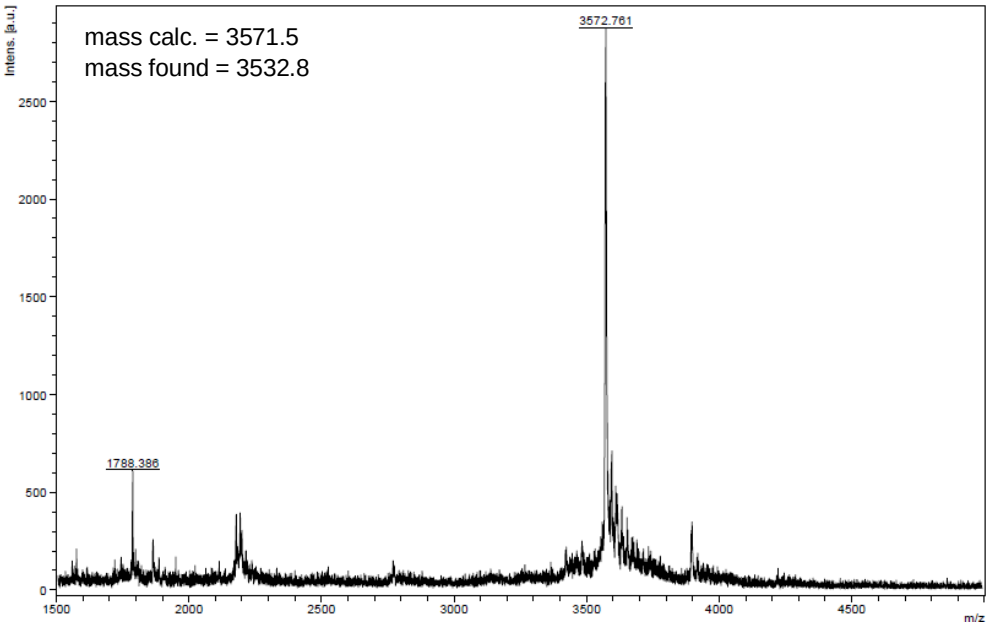
HPLC trace of isolated product 23g (Analytical RP-HPLC, Method-II)



Peak list:

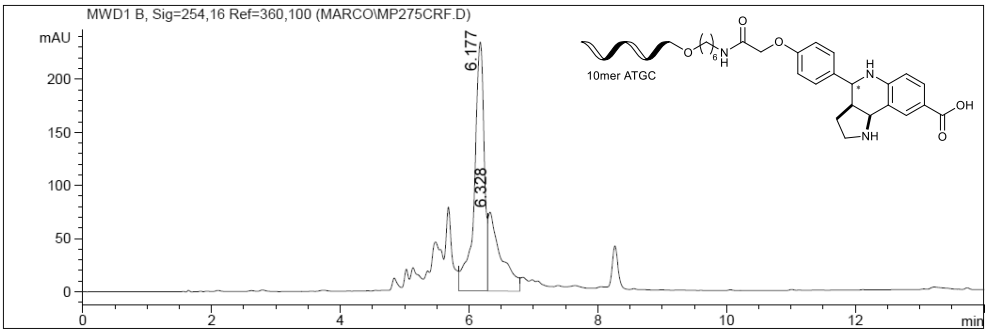
Ret. Time	Width min	Height	Area	Area %
7.256	0.366	214.644	4716.933	100.000

MALDI-MS spectrum of isolated product 23g



DNA conjugate 23h: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-aminobenzoic acid **12t** and *N*-Boc-2,3-dihydro-1H-pyrrole **15a** according to RP-09.

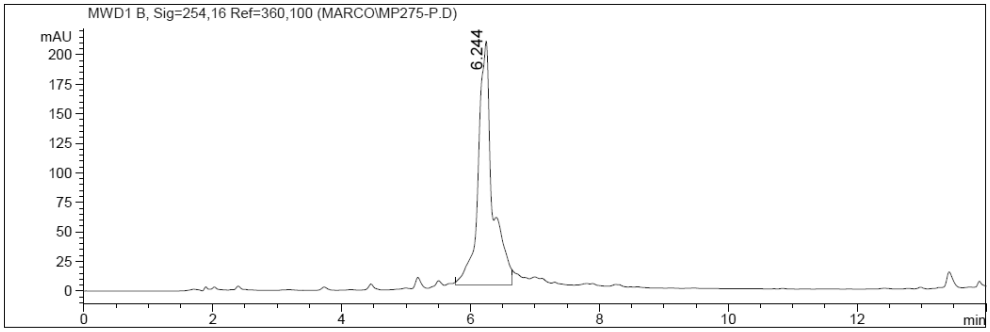
HPLC trace of crude reaction mixture 23h (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.177	0.177	234.443	2494.980	70.214
6.328	0.238	74.245	1058.421	29.786

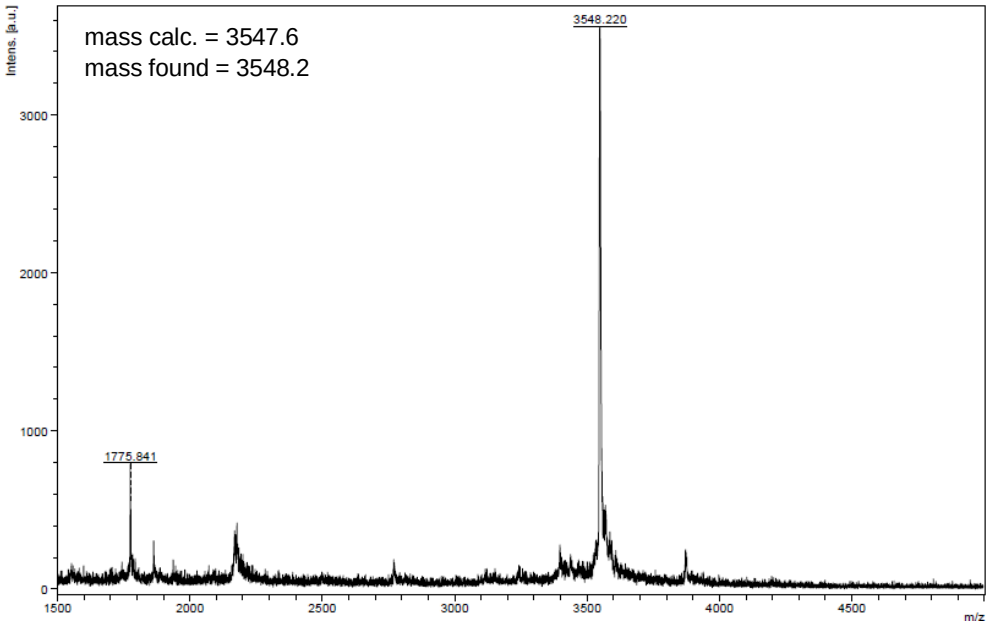
HPLC trace of isolated product 23h (Analytical RP-HPLC, Method-II)



Peak list:

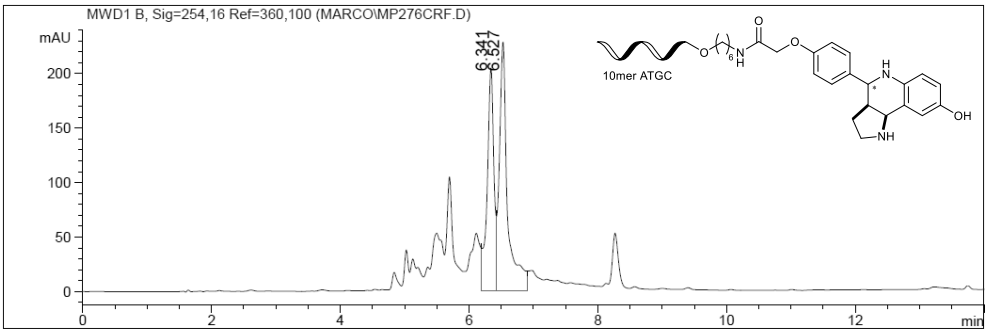
Ret. Time	Width min	Height	Area	Area %
6.244	0.255	206.604	3157.160	100.000

MALDI-MS spectrum of isolated product 23h



DNA conjugate 23i: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-hydroxyaniline **12u** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

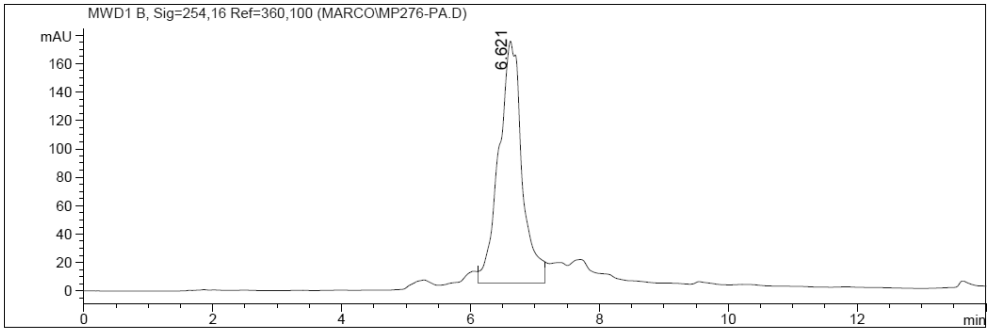
HPLC trace of crude reaction mixture 23i (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.341	0.118	204.855	1456.078	41.891
6.527	0.147	228.536	2019.755	58.109

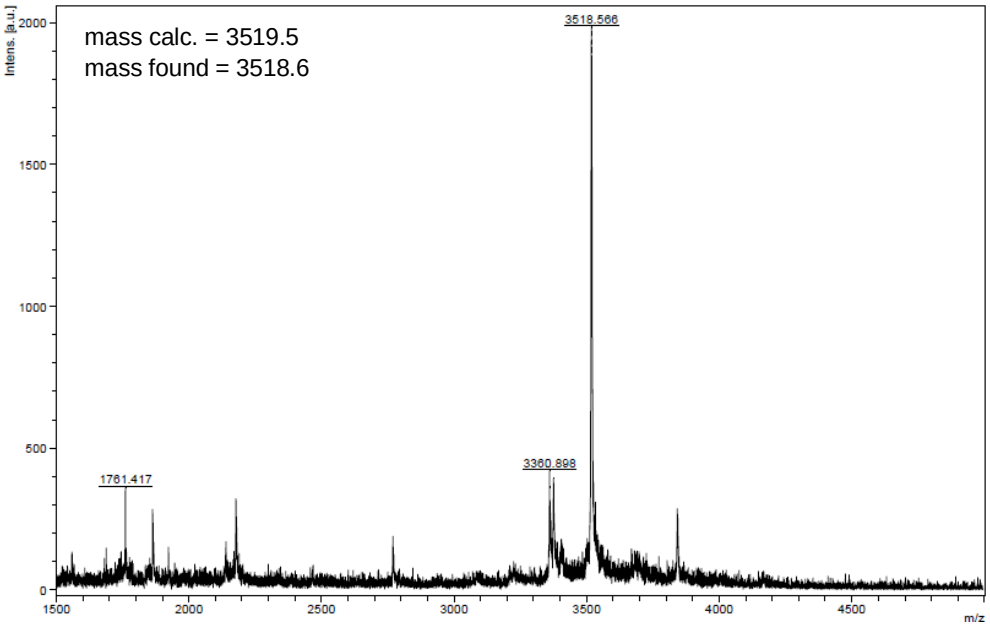
HPLC trace of isolated product 23i (Analytical RP-HPLC, Method-II)



Peak list:

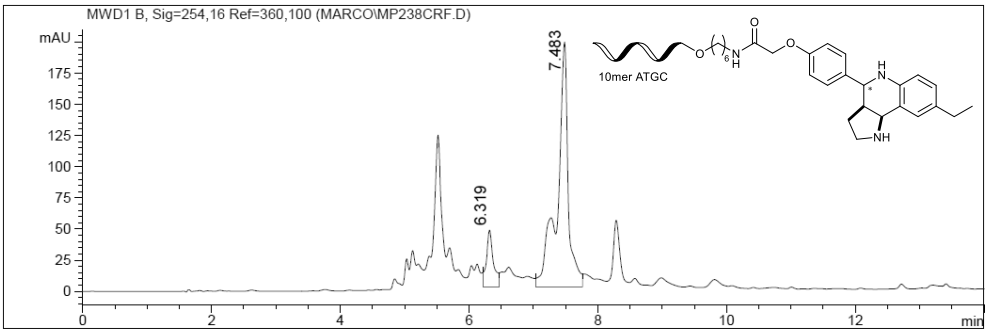
Ret. Time	Width min	Height	Area	Area %
6.621	0.416	170.139	4249.200	100.000

MALDI-MS spectrum of isolated product 23i



DNA conjugate 23j: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-ethylaniline **12b** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

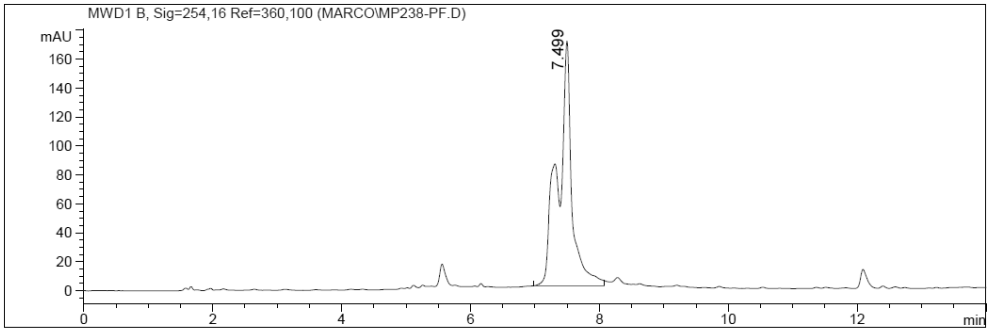
HPLC trace of crude reaction mixture 23j (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.319	0.126	45.753	344.902	13.000
7.483	0.196	196.398	2308.146	87.000

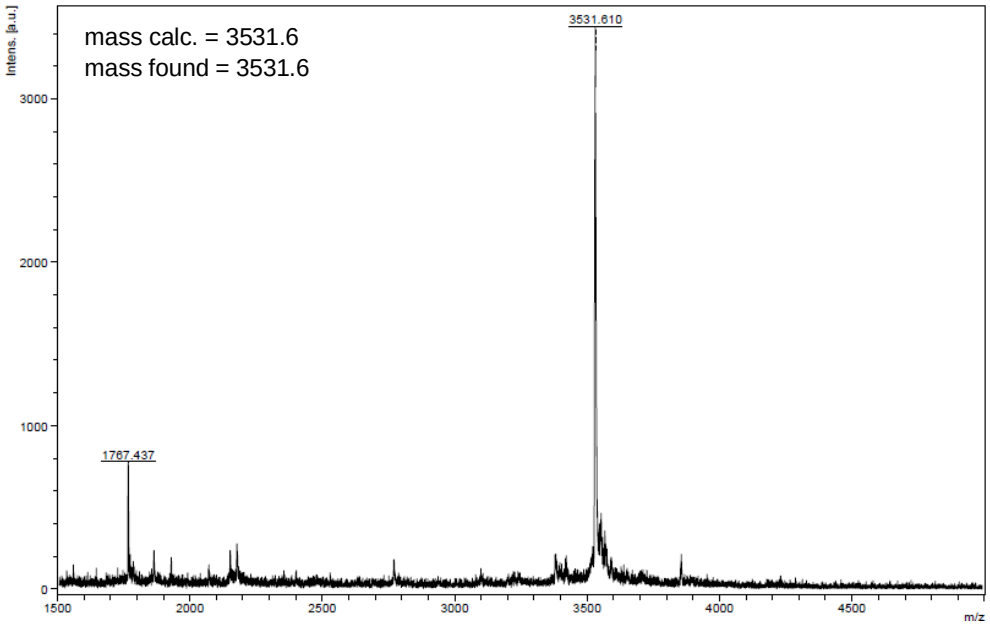
HPLC trace of isolated product 23j (Analytical RP-HPLC, Method-II)



Peak list:

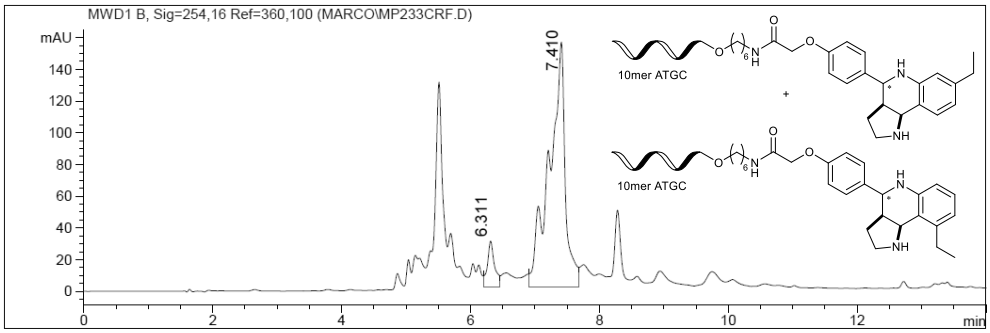
Ret. Time	Width min	Height	Area	Area %
7.499	0.248	169.478	2520.448	100.000

MALDI-MS spectrum of isolated product 23j



DNA conjugate 23k: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-ethylaniline **12c** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

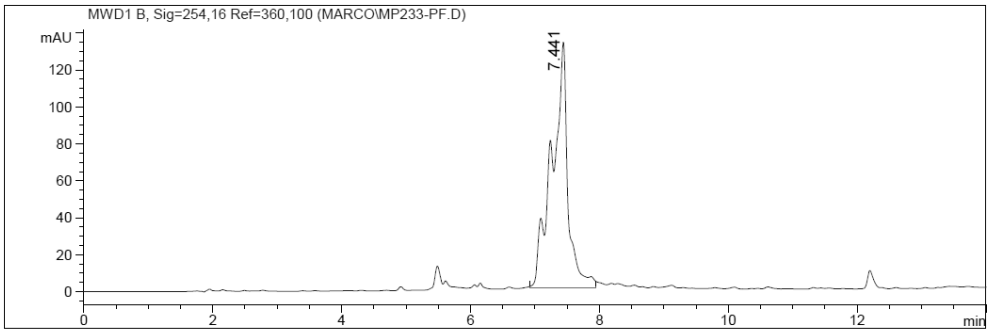
HPLC trace of crude reaction mixture 23k (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.311	0.129	28.811	223.097	7.763
7.410	0.286	154.498	2650.679	92.237

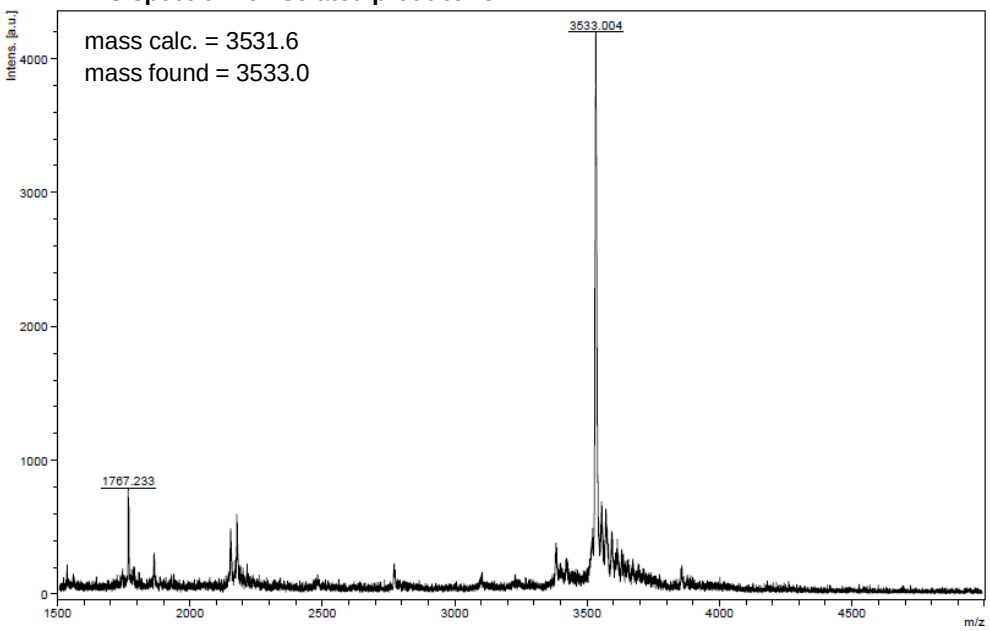
HPLC trace of isolated product 23k (Analytical RP-HPLC, Method-II)



Peak list:

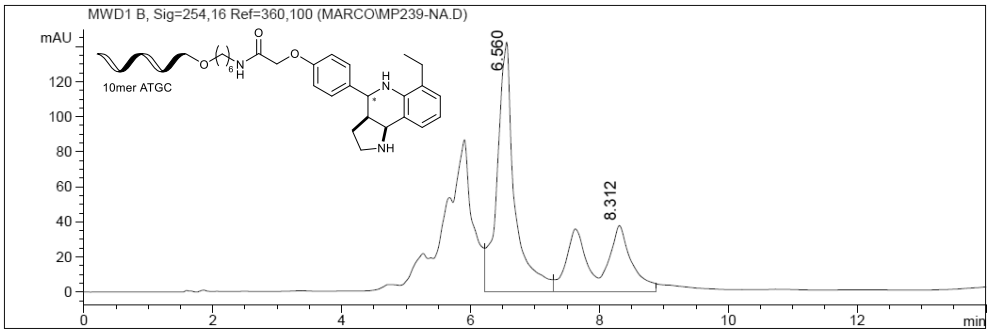
Ret. Time	Width min	Height	Area	Area %
7.441	0.286	133.129	2283.371	100.000

MALDI-MS spectrum of isolated product 23k



DNA conjugate 23l: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-ethylaniline **12d** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

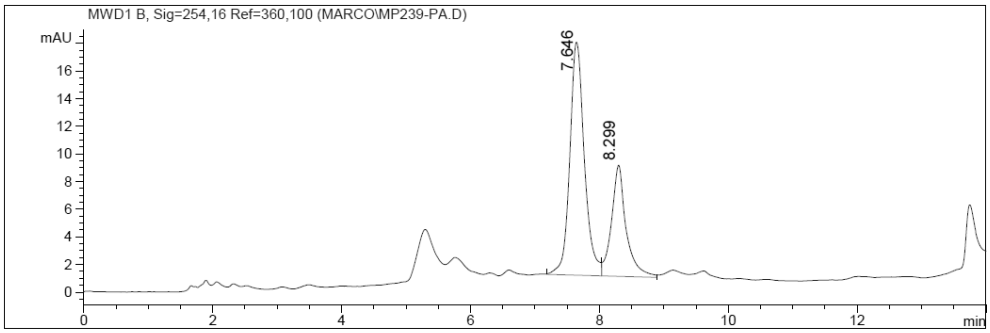
HPLC trace of crude reaction mixture 23l (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.560	0.312	142.420	2666.813	61.419
8.312	0.740	37.744	1675.209	38.581

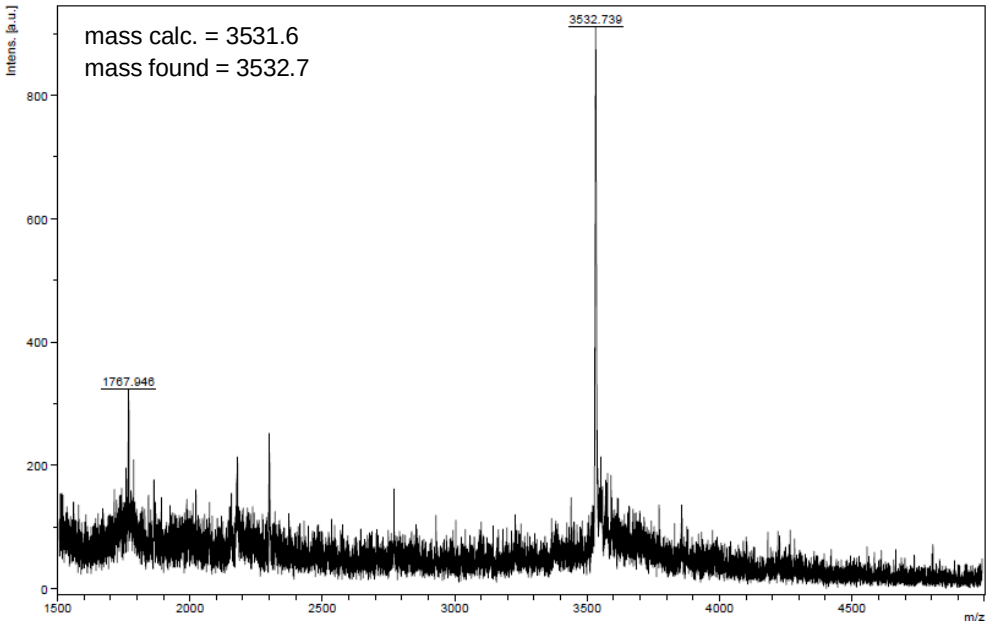
HPLC trace of isolated product 23l (Analytical RP-HPLC, Method-II)



Peak list:

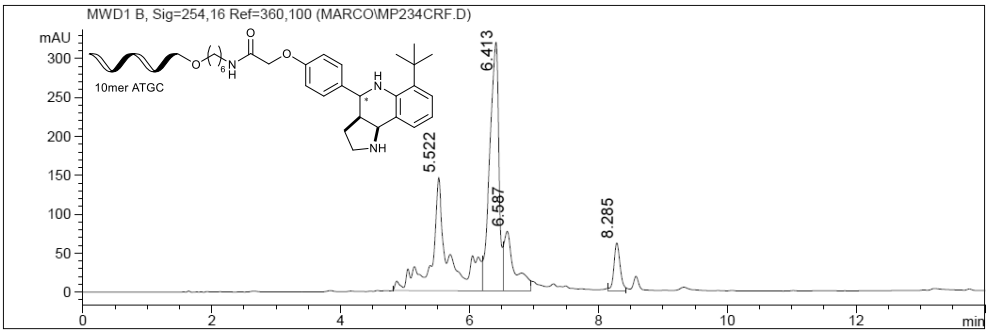
Ret. Time	Width min	Height	Area	Area %
7.646	0.233	16.867	263.930	67.652
8.299	0.221	8.049	126.196	32.348

MALDI-MS spectrum of isolated product 23l



DNA conjugate 23m: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-*tert* butylaniline **12k** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

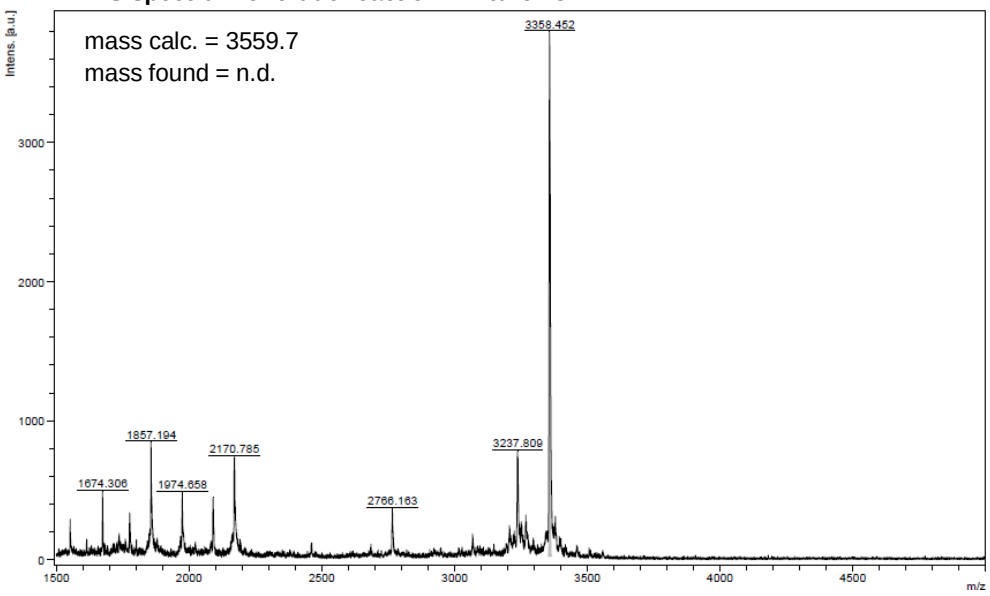
HPLC trace of crude reaction mixture 23m (Analytical RP-HPLC, Method-II)



Peak list:

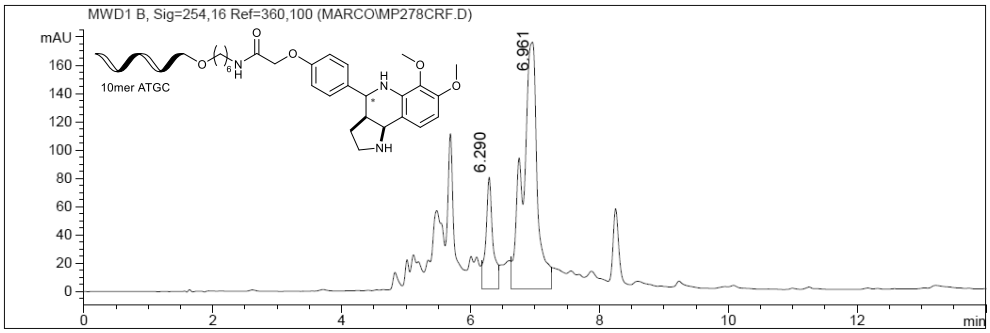
Ret. Time	Width min	Height	Area	Area %
5.522	0.319	145.795	2793.278	38.528
6.413	0.164	320.226	3144.597	43.373
6.587	0.194	76.655	890.530	12.283
8.285	0.113	62.314	421.676	5.816

MALDI-MS spectrum of crude reaction mixture 23m



DNA conjugate 23n: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2,3-dimethoxyaniline **12m** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

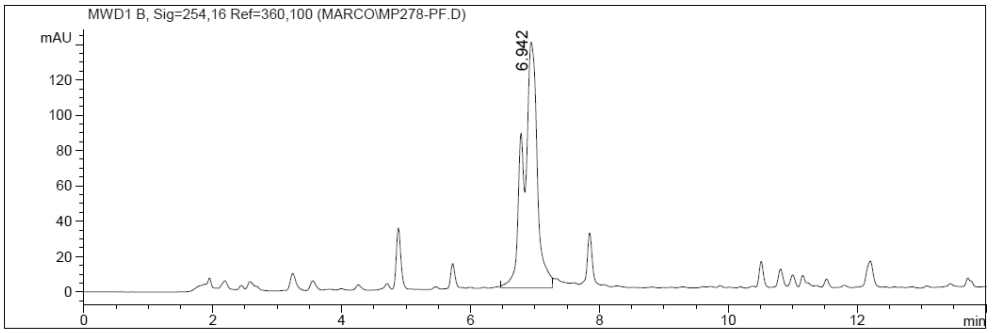
HPLC trace of crude reaction mixture 23n (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.290	0.127	79.191	605.753	18.252
6.961	0.259	174.555	2713.016	81.748

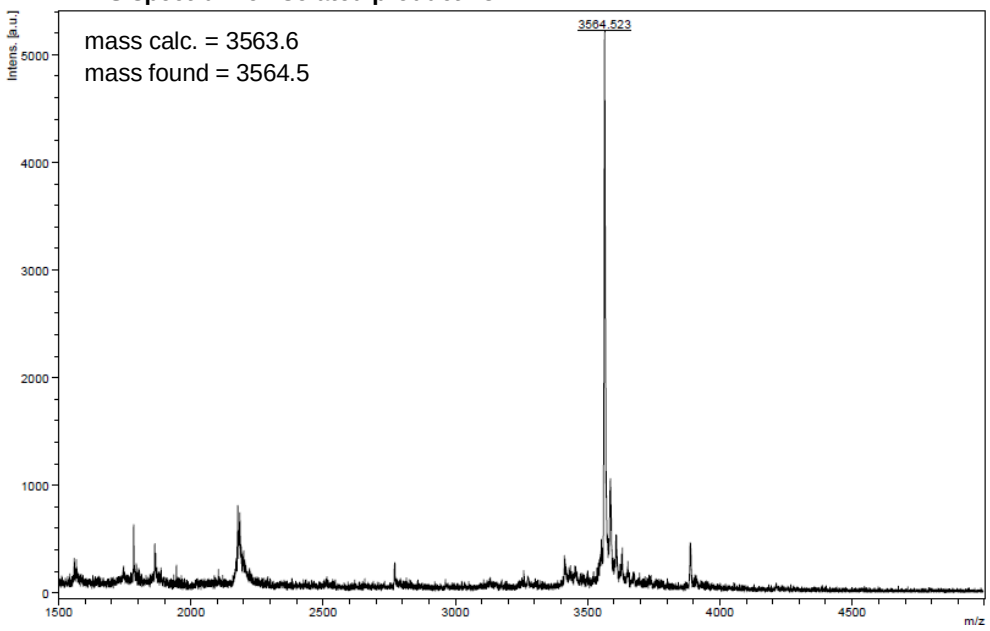
HPLC trace of isolated product 23n (Analytical RP-HPLC, Method-II)



Peak list:

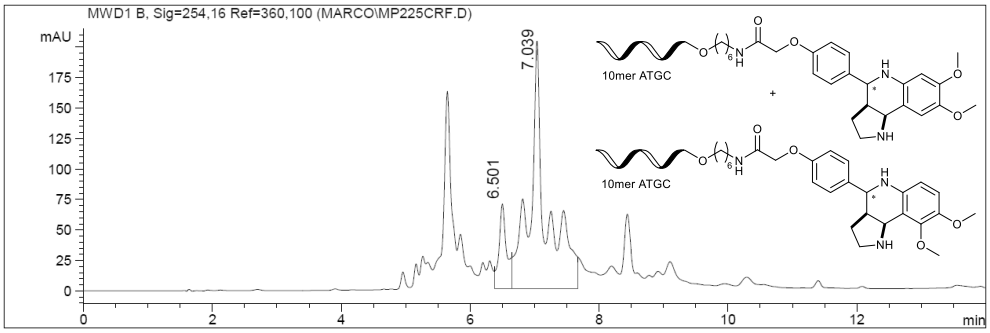
Ret. Time	Width min	Height	Area	Area %
6.942	0.248	139.371	2069.797	100.000

MALDI-MS spectrum of isolated product 23n



DNA conjugate 23o: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3,4-dimethoxyaniline **12l** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

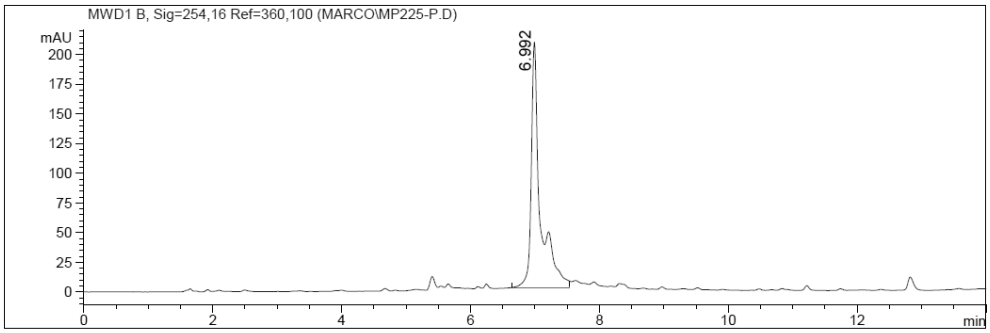
HPLC trace of crude reaction mixture 23o (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.501	0.140	69.709	584.579	14.143
7.039	0.290	203.822	3548.664	85.857

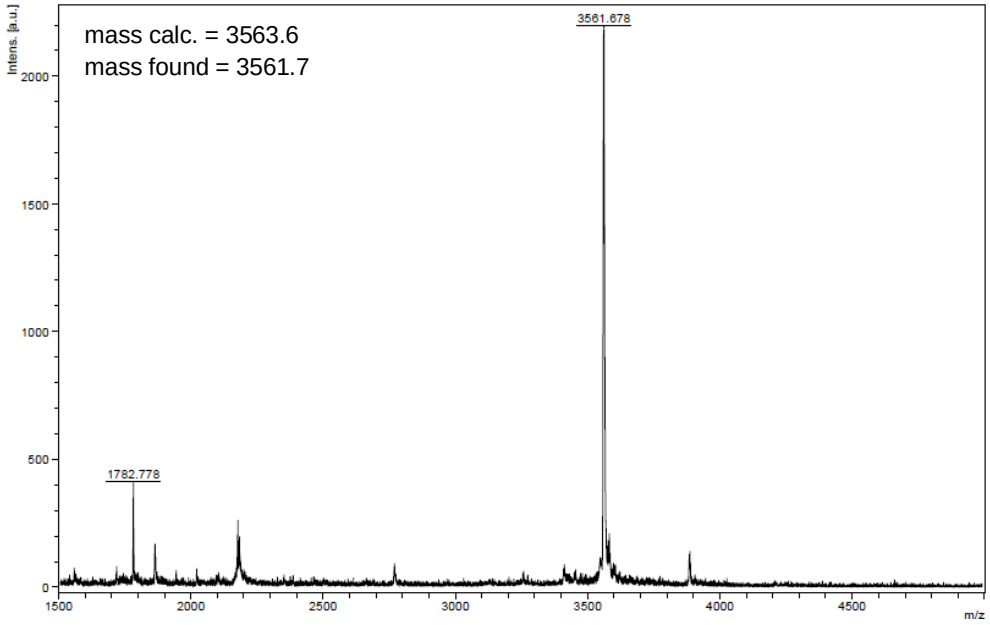
HPLC trace of isolated product 23o (Analytical RP-HPLC, Method-II)



Peak list:

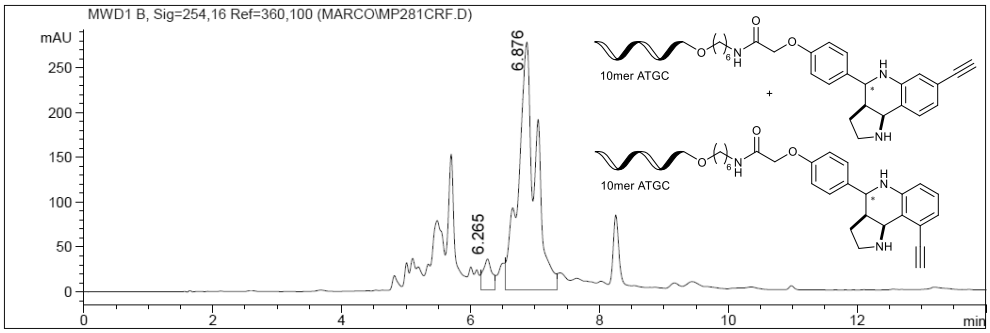
Ret. Time	Width min	Height	Area	Area %
6.992	0.162	207.279	2009.840	100.000

MALDI-MS spectrum of isolated product 23o



DNA conjugate 23p: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-ethynylaniline **12o** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

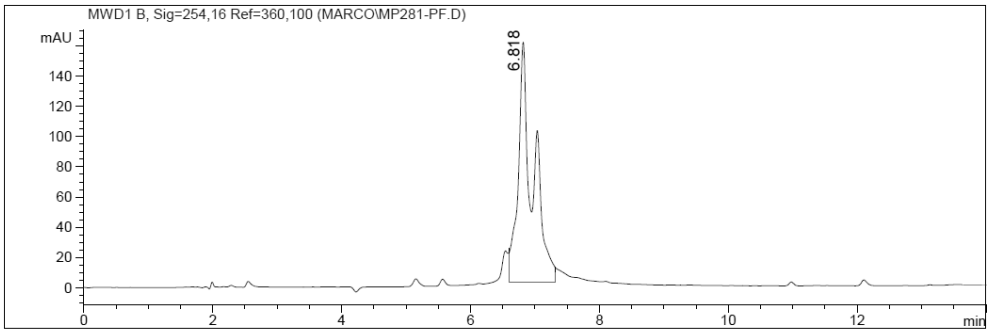
HPLC trace of crude reaction mixture 23p (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.265	0.156	34.292	321.008	5.862
6.876	0.311	276.447	5154.825	94.138

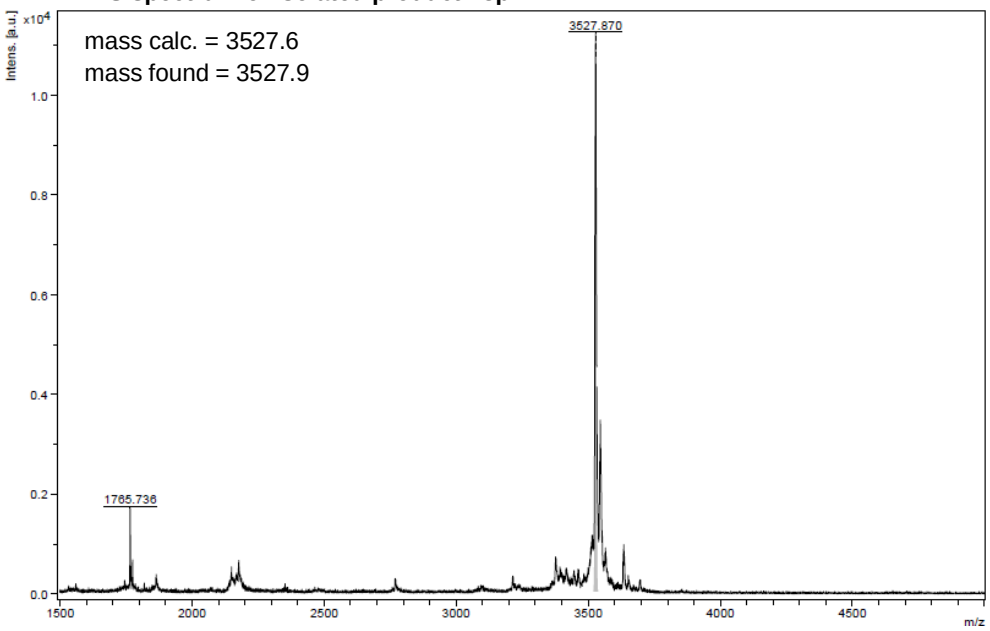
HPLC trace of isolated product 23p (Analytical RP-HPLC, Method-II)



Peak list:

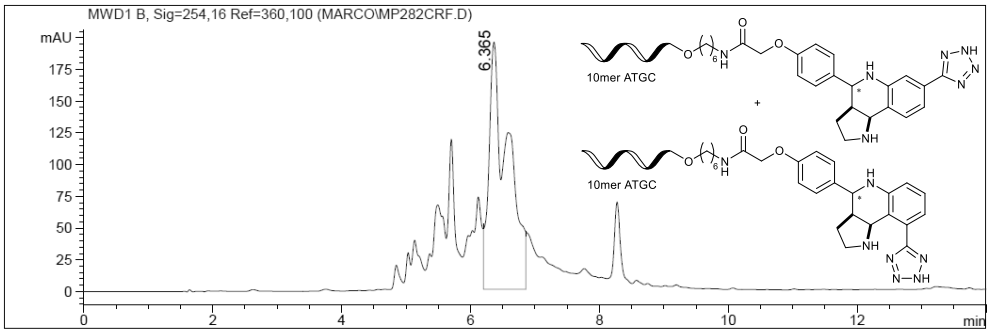
Ret. Time	Width min	Height	Area	Area %
6.818	0.257	158.818	2453.143	100.000

MALDI-MS spectrum of isolated product 23p



DNA conjugate 23q: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 3-(2H-tetrazol-5-yl)aniline **12p** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

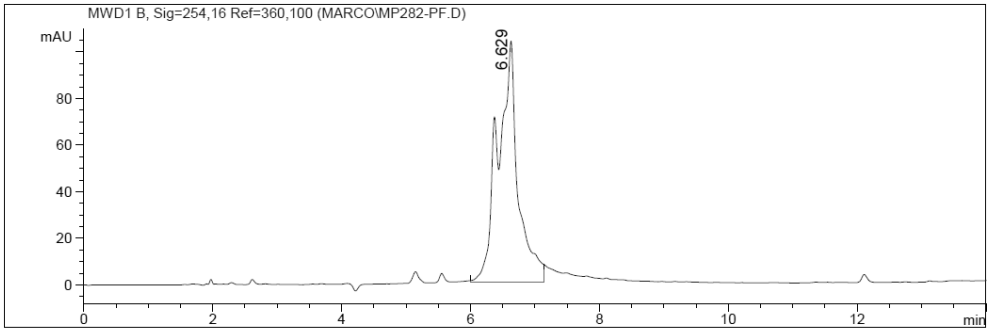
HPLC trace of crude reaction mixture 23q (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.365	0.340	194.807	3973.136	100.000

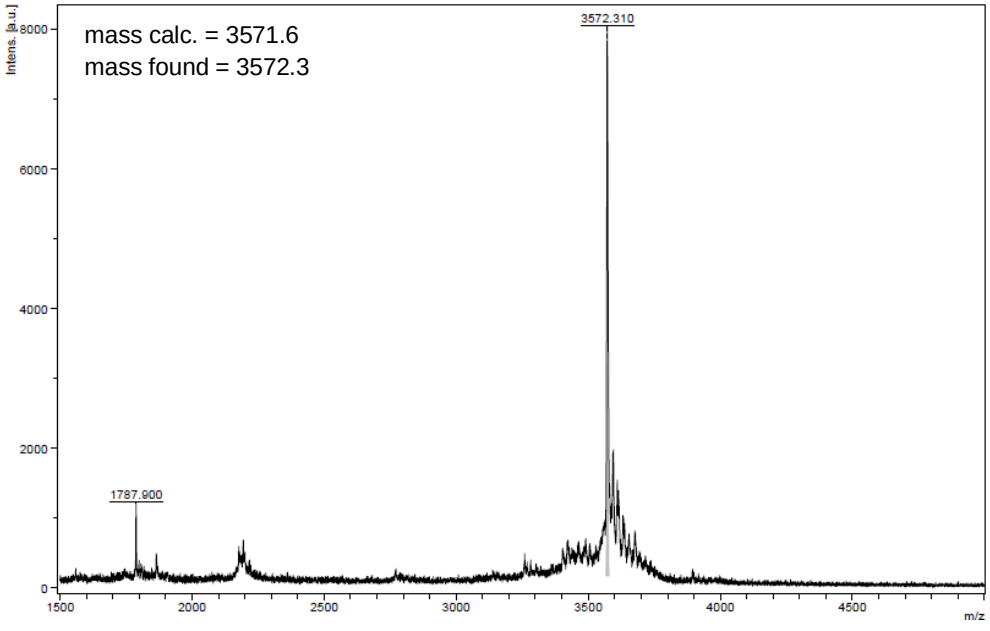
HPLC trace of isolated product 23q (Analytical RP-HPLC, Method-II)



Peak list:

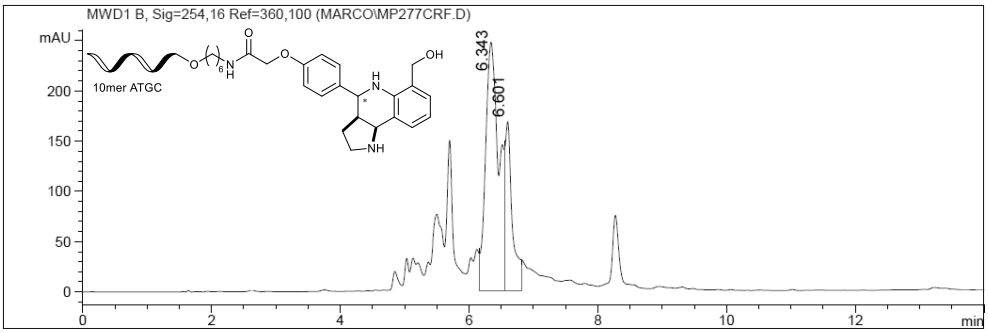
Ret. Time	Width min	Height	Area	Area %
6.629	0.359	103.453	2230.785	100.000

MALDI-MS spectrum of isolated product 23q



DNA conjugate 23r: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-(hydroxyl-methyl)aniline **12v** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

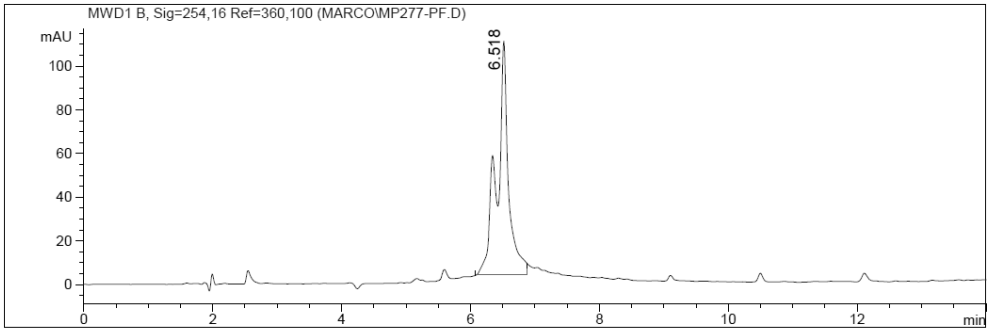
HPLC trace of crude reaction mixture 23r (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.343	0.245	247.679	3641.017	75.375
6.601	0.118	168.657	1189.490	24.625

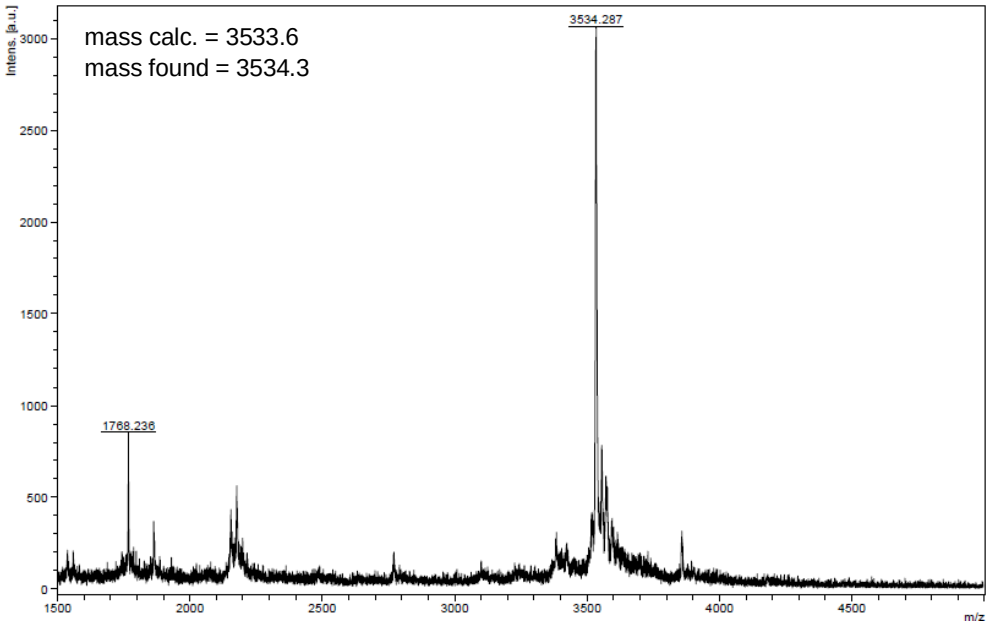
HPLC trace of isolated product 23r (Analytical RP-HPLC, Method-II)



Peak list:

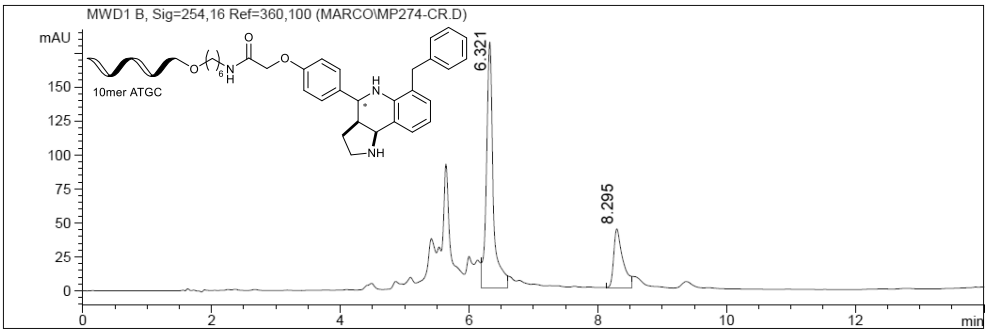
Ret. Time	Width min	Height	Area	Area %
6.518	0.207	107.314	1331.752	100.000

MALDI-MS spectrum of isolated product 23r



DNA conjugate 23s: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 2-benzylaniline **12w** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

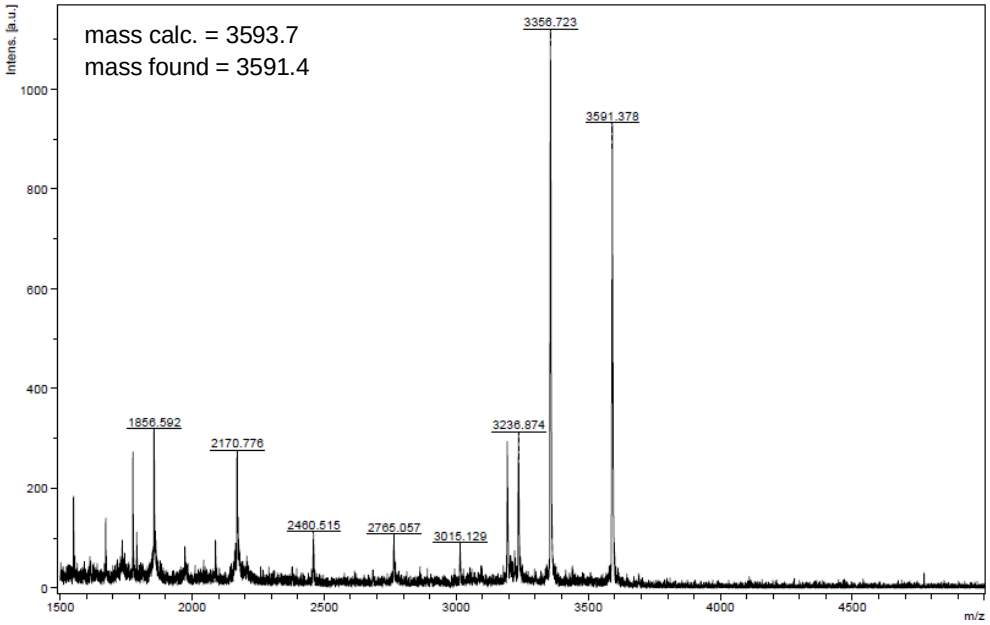
HPLC trace of crude reaction mixture 23s (Analytical RP-HPLC, Method-II)



Peak list:

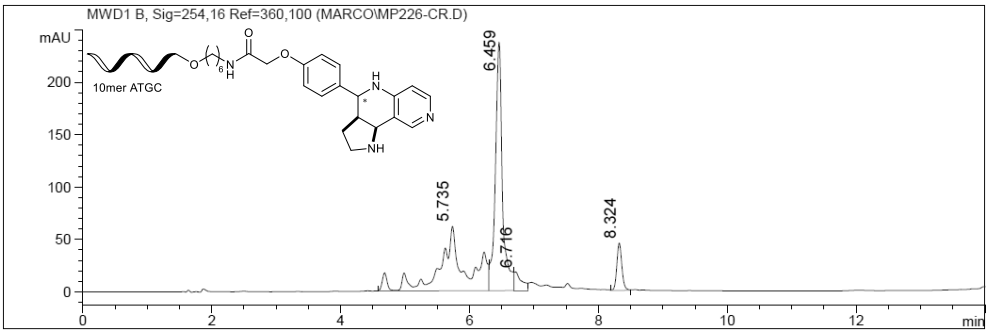
Ret. Time	Width min	Height	Area	Area %
6.321	0.121	181.120	1319.821	75.428
8.295	0.165	43.493	429.965	24.572

MALDI-MS spectrum of crude reaction mixture 23s



DNA conjugate 23t: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-Aminopyridine **12q** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

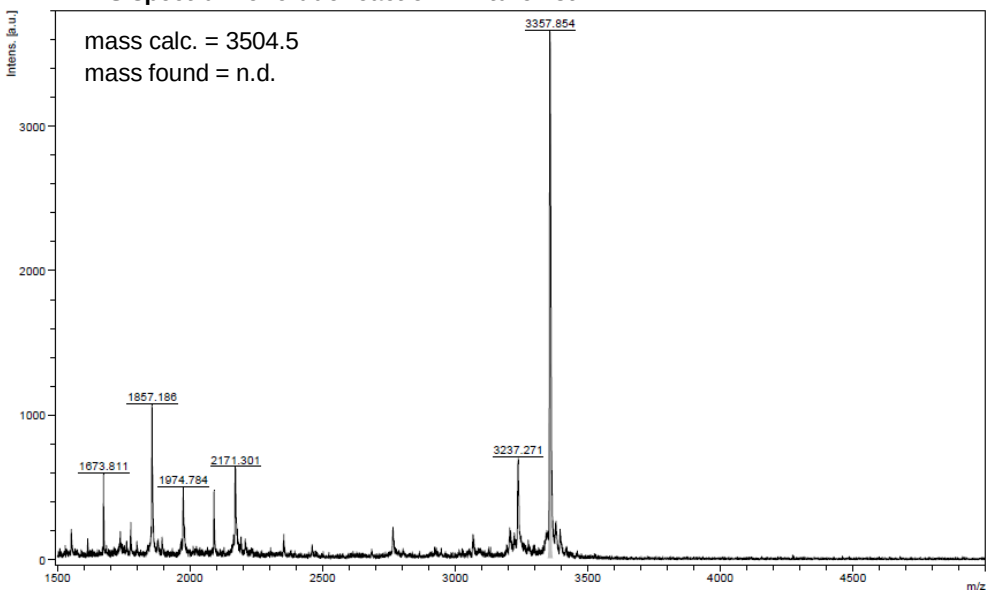
HPLC trace of crude reaction mixture 23t (Analytical RP-HPLC, Method-II)



Peak list:

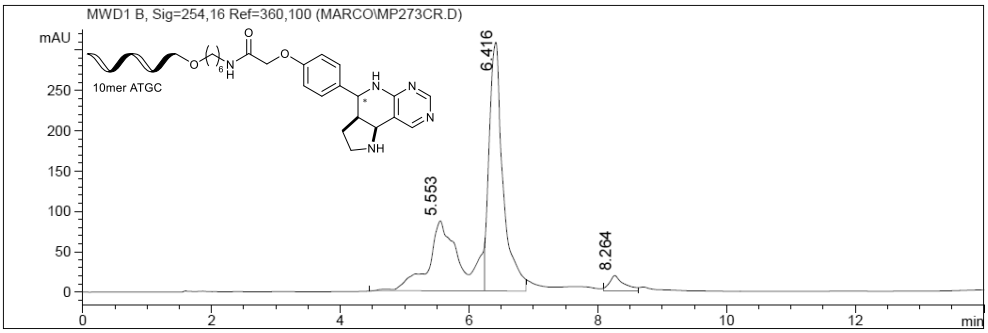
Ret. Time	Width min	Height	Area	Area %
5.735	0.451	61.583	1664.991	43.046
6.459	0.127	237.525	1817.064	46.977
6.716	0.133	17.753	141.318	3.654
8.324	0.090	45.401	244.597	6.324

MALDI-MS spectrum of crude reaction mixture 23t



DNA conjugate 23u: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with 4-Aminopyrimidine **12x** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

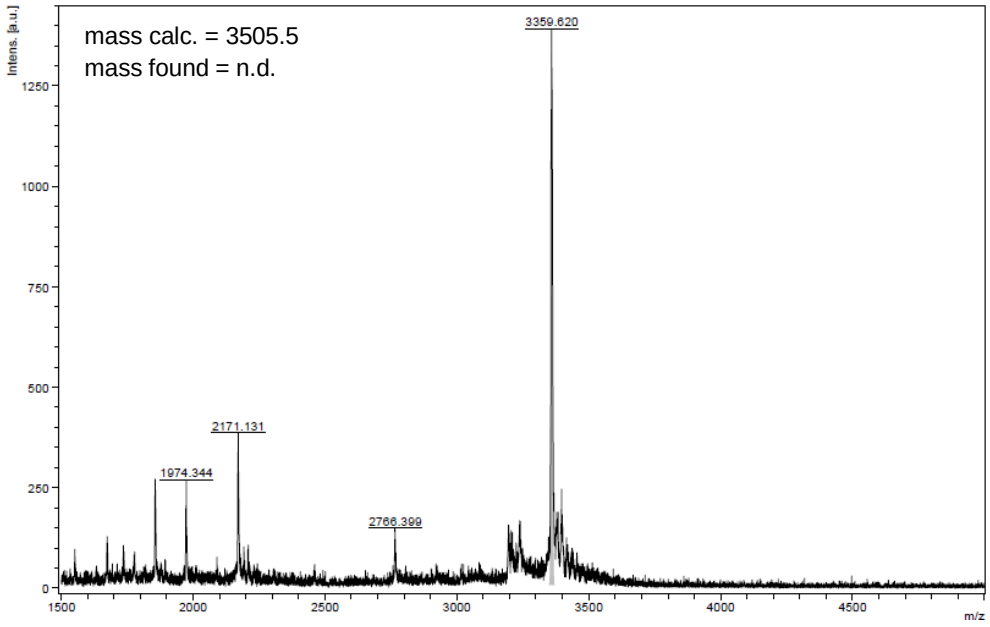
HPLC trace of crude reaction mixture 23u (Analytical RP-HPLC, Method-II)



Peak list:

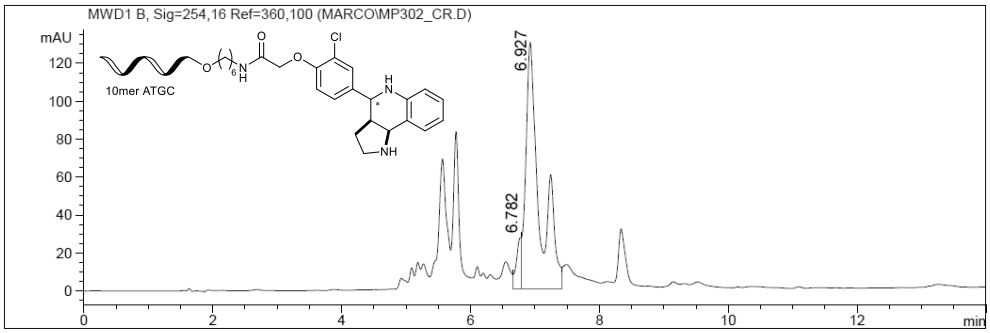
Ret. Time	Width min	Height	Area	Area %
5.553	0.585	86.666	3044.036	38.275
6.416	0.248	308.370	4595.420	57.781
8.264	0.271	19.285	313.670	3.944

MALDI-MS spectrum of crude reaction mixture 23u



DNA conjugate 23v: CPG-coupled 10mer ATGC-aldehyde conjugate **15b** was reacted with aniline **12a** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

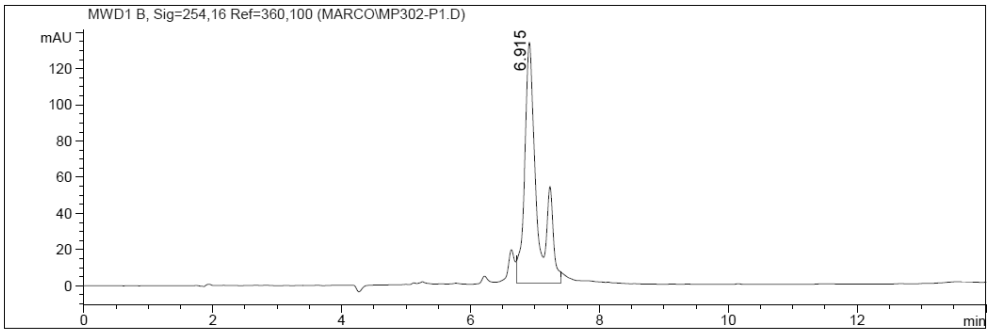
HPLC trace of crude reaction mixture 23v (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.782	0.091	27.097	147.754	7.261
6.927	0.242	130.151	1887.230	92.739

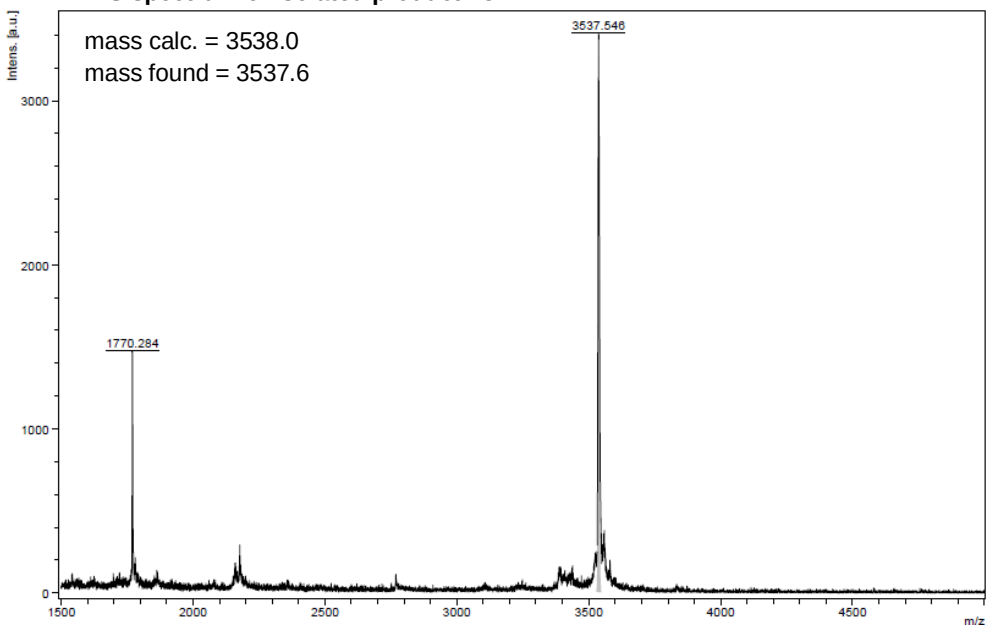
HPLC trace of isolated product 23v (Analytical RP-HPLC, Method-II)



Peak list:

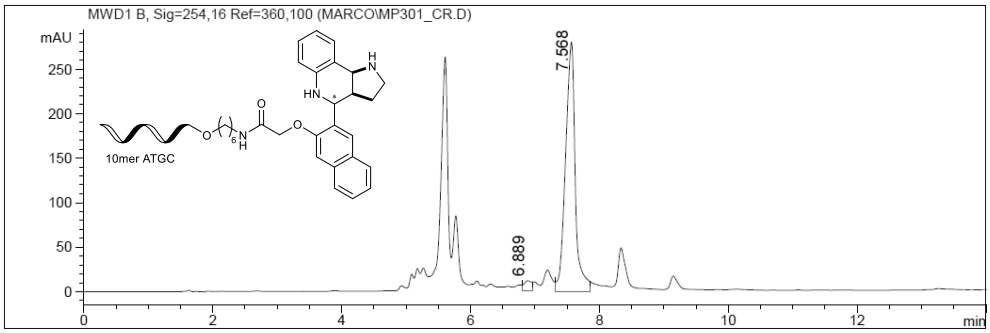
Ret. Time	Width min	Height	Area	Area %
6.915	0.227	133.464	1821.646	100.000

MALDI-MS spectrum of isolated product 23v



DNA conjugate 23w: CPG-coupled 10mer ATGC-aldehyde conjugate **15c** was reacted with aniline **12a** and *N*-Boc-2,3-dihydro-1H-pyrrole **20** according to RP-09.

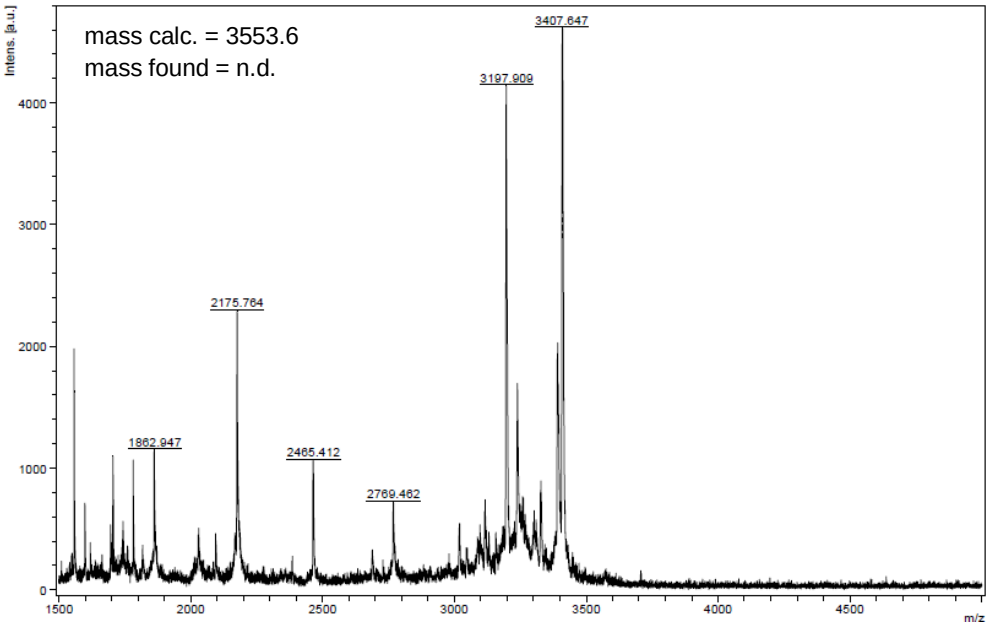
HPLC trace of crude reaction mixture 23w (Analytical RP-HPLC, Method-II)



Peak list:

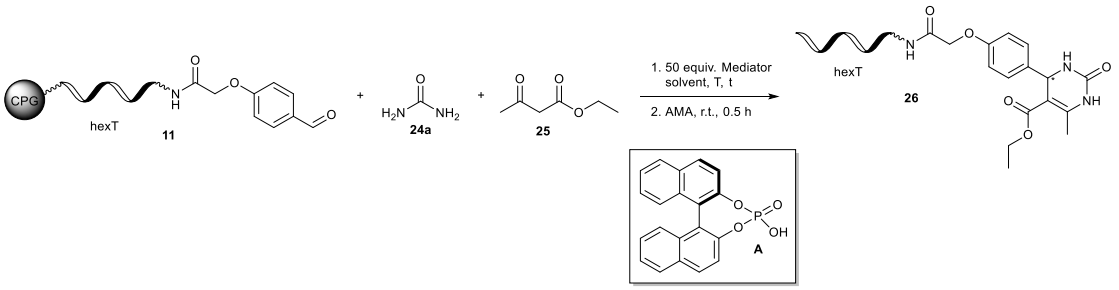
Ret. Time	Width min	Height	Area	Area %
6.889	0.145	11.785	102.258	3.377
7.568	0.174	280.383	2925.668	96.623

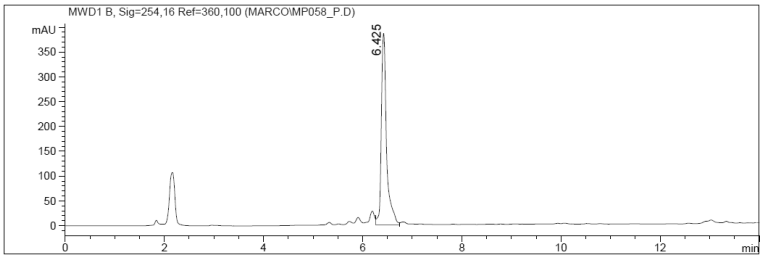
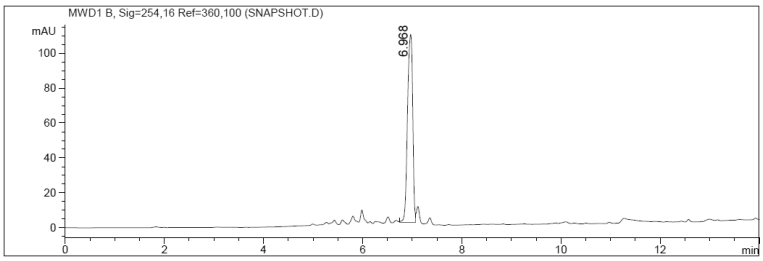
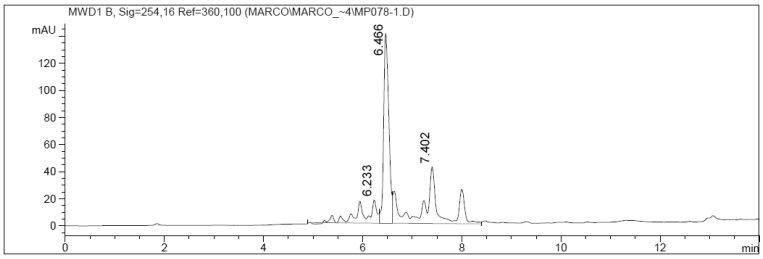
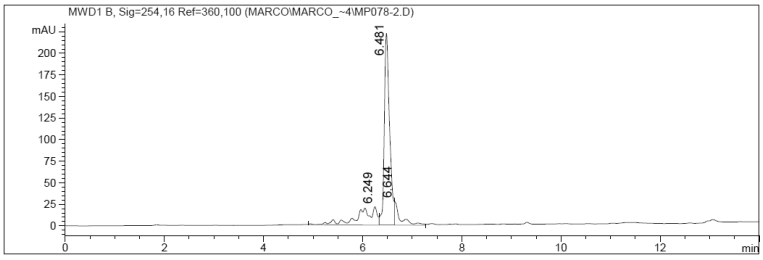
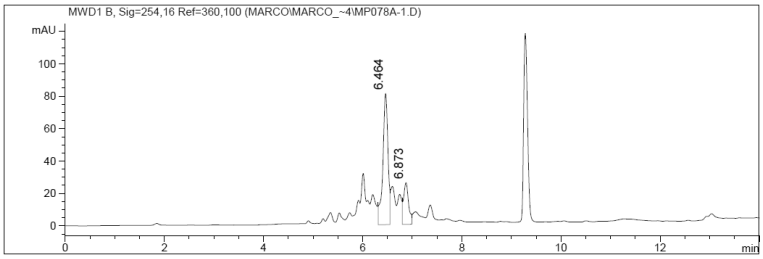
MALDI-MS spectrum of isolated product 23w



(*R*)-(-)-BNDHP-mediated Biginelli reaction on CPG-coupled oligonucleotides

Table S11 Optimization of (*R*)-(-)-BNDHP -mediated Biginelli reaction on CPG-coupled hexT.[a]

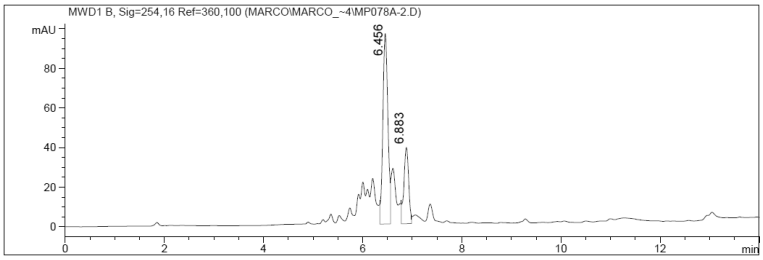


Entry	Reaction conditions[b]	HPLC trace of crude reaction mixture[c]
1	hexT-aldehyde conjugate **11**	
2	hexT-dihydropyrimidinone conjugate **26**	
3	50 equiv. $Yb(OTf)_3$ THF, r.t., 20 h => conversion <5 %	
4	50 equiv. (*R*)-(-)-BNDHP **A** THF, r.t., 20 h => conversion < 5%	
5	50 equiv. ***Yb(OTf)₃*** THF, ***50 °C***, 20 h => conversion 24 %	

6

50 equiv. ***(R)-(-)-BNDHP A***
THF, ***50 °C***, 20 h

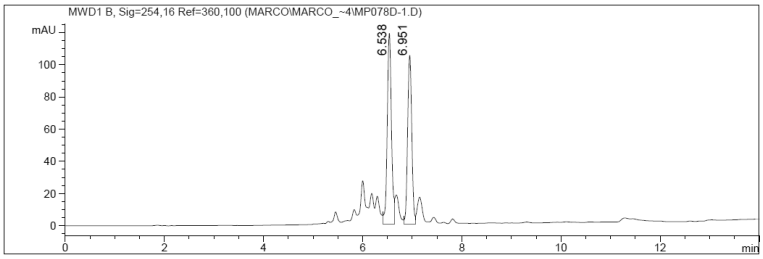
=> conversion 28 %



7

50 equiv. ***Yb(OTf)$_3$***
EtOH, ***r.t.***, 20 h

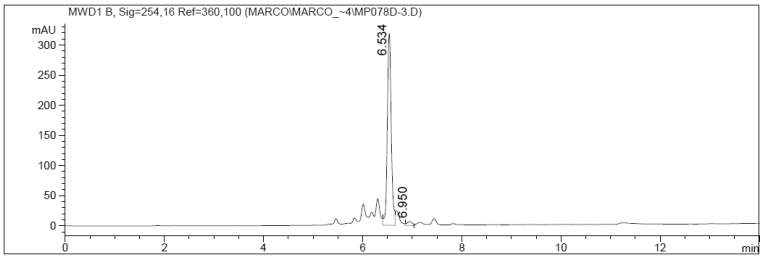
=> conversion 47 %



8

50 equiv. ***Mg(ClO$_4$)$_2$***
EtOH, ***r.t.***, 20 h

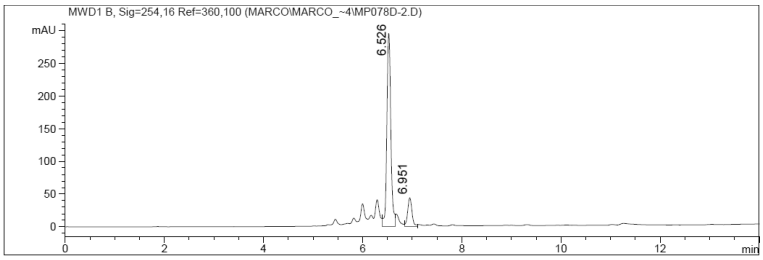
=> conversion <5 %



9

50 equiv. ***(R)-(-)-BNDHP A***
EtOH, ***r.t.***, 20 h

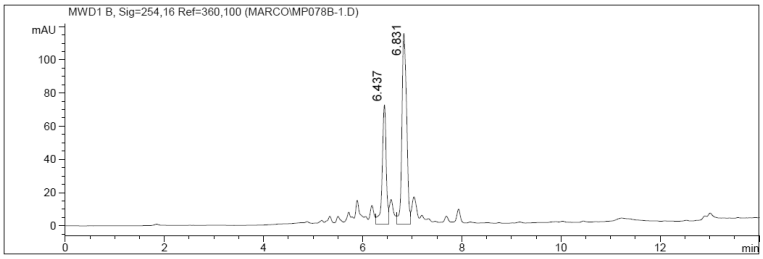
=> conversion 13 %



10

50 equiv. ***Yb(OTf)$_3$***
EtOH, ***50 °C***, 20 h

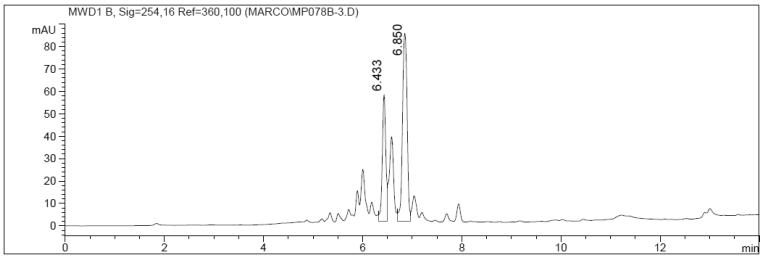
=> conversion 65 %



11

50 equiv. ***Mg(ClO$_4$)$_2$***
EtOH, ***50 °C***, 20 h

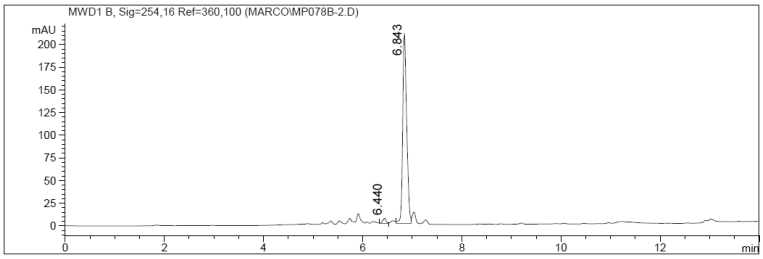
=> conversion 65 %

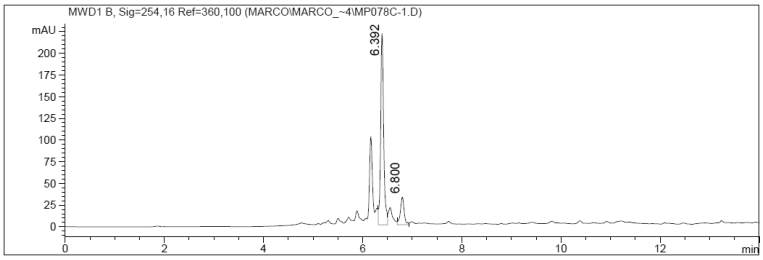
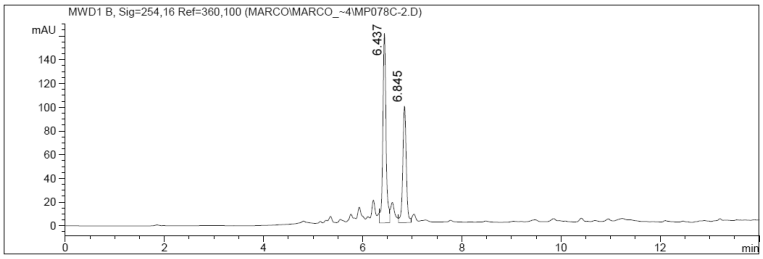


12

50 equiv. ***(R)-(-)-BNDHP A***
EtOH, ***50 °C***, 20 h

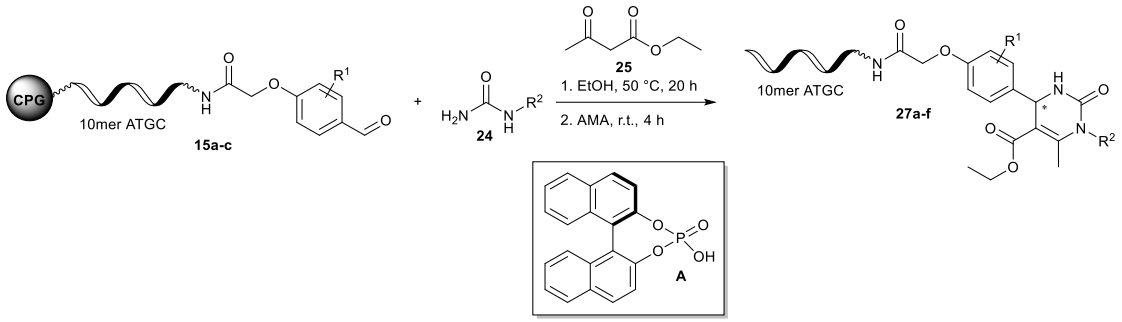
=> conversion 97 %



13	50 equiv. (*R*)-(-)-BNDHP **A** EtOH, 50 °C, ***4 h*** => conversion 14 %	
14	50 equiv. (*R*)-(-)-BNDHP **A** EtOH, 50 °C, ***8 h*** => conversion 40 %	

[a] CPG-coupled hexT aldehyde conjugate **11** (20 nmol) was suspended in indicated solvent with urea **24a** (500 equiv.) and mediator (50 equiv., 1 µmol) each dissolved or suspended in 30 µL of indicated solvent and ethyl acetoacetate **25** (500 equiv.), reaction mixture was shaken at indicated temperature for 20 h. Afterwards AMA (30% aqueous ammonia / 40% aqueous methylamine, 1:1 (vol/vol)) at ambient temperature for 0.5 h. [b] parameters that were changed are in bold and italic. [c] Analytical RP-HPLC, Method-I.

Table S12 – Scope of (*R*)-(-)-BNDHP **A**-mediated Biginelli reaction on CPG-coupled 10mer ATGC oligonucleotide-aldehyde conjugates **15** with ureas **24** and ethyl acetoacetate **25**.[a]



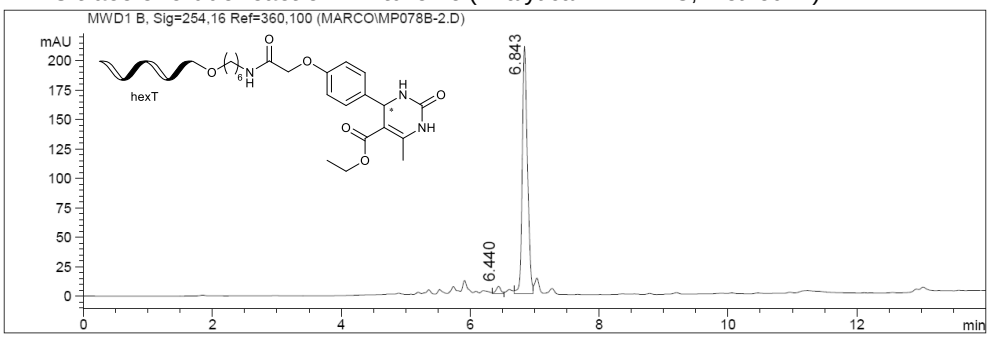
Entry	Product	DNA-aldehyde conjugate	Urea	Conversion [%][b]	$Mass_{calc.}$ $Mass_{found}$[d]
1	**27a**	**15a**	**24a**	90	3513.5 3513.3
2	**27b**	**15a**	**24b**	59	3541.5 3540.0
3	**27c**	**15a**	**24c**	10 (75[c,d])	3589.6 3593.6
4	**27d**	**15a**	**24d**	85	3603.6 3602.9
5	**27e**	**15b**	**24a**	92	3547.9 3547.9
6	**27f**	**15c**	**24a**	n.d.	3563.6 n.d.

[a] CPG-coupled ATGC aldehyde conjugate **15** (20 nmol) was suspended with urea **24** (500 equiv.) and (*R*)-(-)-BNDHP **A** (50 equiv., 1 µmol) each dissolved in 30 µL of ethanol and ethyl acetoacetate **25** (500 equiv.), reaction mixture was shaken at 50 °C for 20 h. Afterwards AMA (30% aqueous ammonia / 40% aqueous methylamine, 1:1 (vol/vol)) at ambient temperature for four h. [b] Determined by analytical RP-HPLC analysis. [c] 200 equiv. of (R)-(-)-BNDHP **A** were used. [d] reaction was performed at 50 °C for 44 h. [d] Measured by MALDI-MS. 10mer ATGC = 5'-GTC ATG ATC T-3', n.d. = not detected.

Products of Biginelli reaction on CPG-coupled oligonucleotide-aldehyde conjugate

DNA conjugate 26: CPG-coupled 10mer hexT-aldehyde conjugate **11** was reacted with urea **24a** and ethyl acetoacetate **25** according to RP-10.

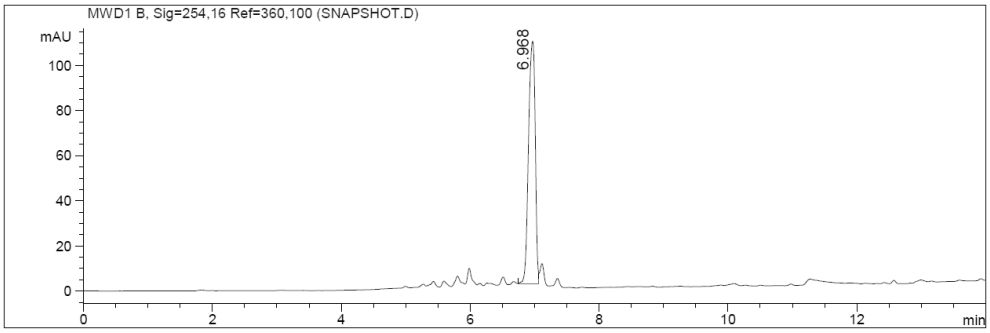
HPLC trace of crude reaction mixture 26 (Analytical RP-HPLC, Method-III)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.440	0.087	6.100	31.898	2.653
6.843	0.093	210.296	1170.318	97.347

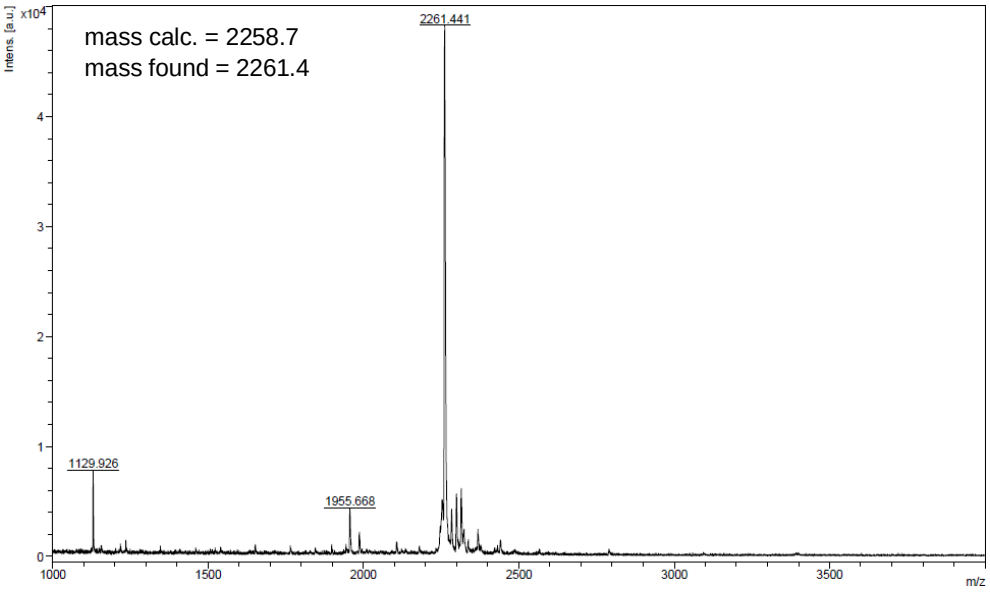
HPLC trace of isolated product 26 (Analytical RP-HPLC, Method-II)



Peak list:

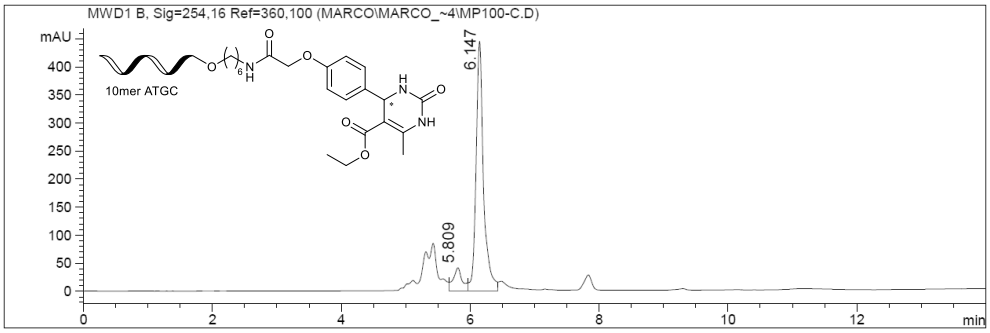
Ret. Time	Width min	Height	Area	Area %
6.968	0.120	107.631	778.136	100.000

MALDI-MS spectrum of isolated product 26



DNA conjugate 27a: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with urea **24a** and ethyl acetoacetate **25** according to RP-10.

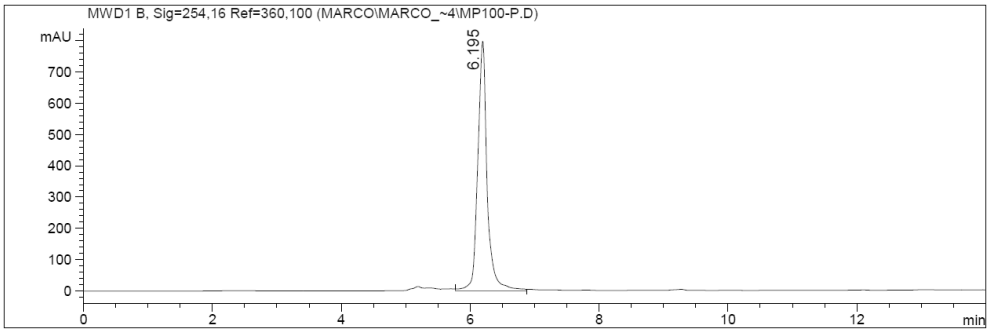
HPLC trace of crude reaction mixture 27a (Analytical RP-HPLC, Method-III)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.809	0.158	41.502	394.660	9.946
6.147	0.134	445.623	3573.551	90.054

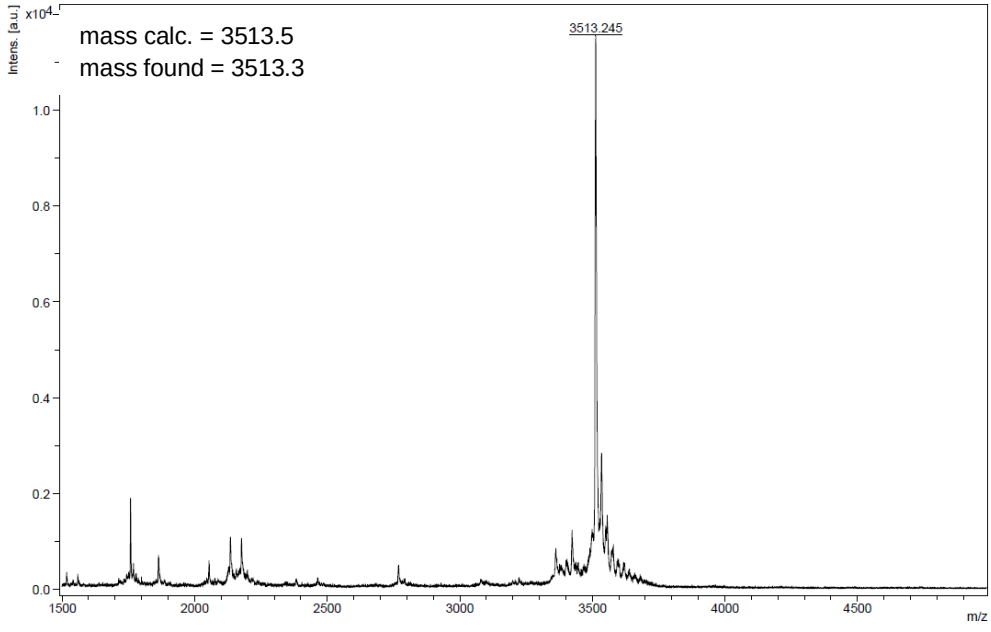
HPLC trace of isolated product 27a (Analytical RP-HPLC, Method-III)



Peak list:

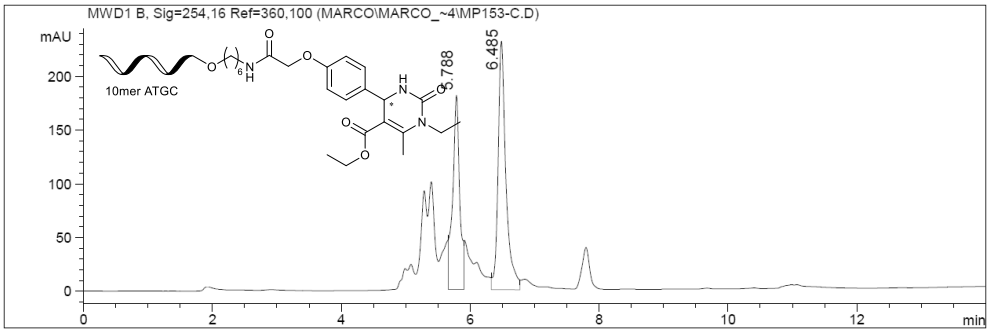
Ret. Time	Width min	Height	Area	Area %
6.195	0.144	796.682	8070.688	100.000

MALDI-MS spectrum of isolated product 27a



DNA conjugate 27b: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with *N*-ethylurea **24b** and ethyl acetoacetate **25** according to RP-10.

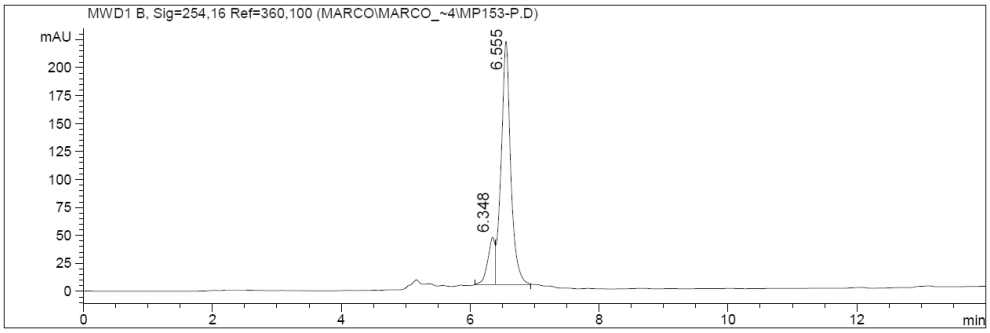
HPLC trace of crude reaction mixture 27b (Analytical RP-HPLC, Method-III)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.788	0.127	181.070	1382.508	41.493
6.485	0.140	232.049	1949.426	58.507

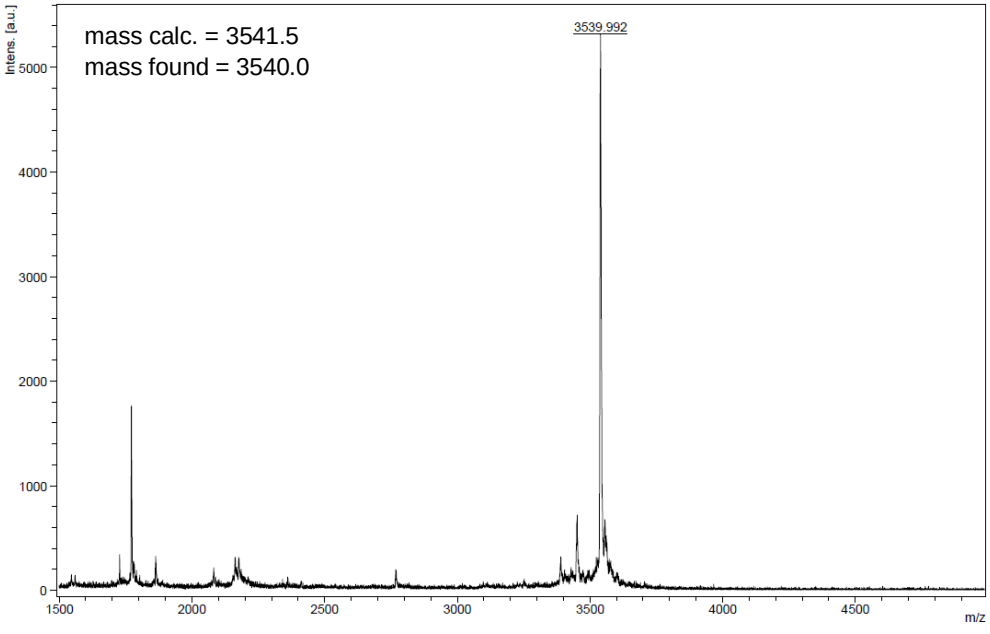
HPLC trace of isolated product 27b (Analytical RP-HPLC, Method-III)



Peak list:

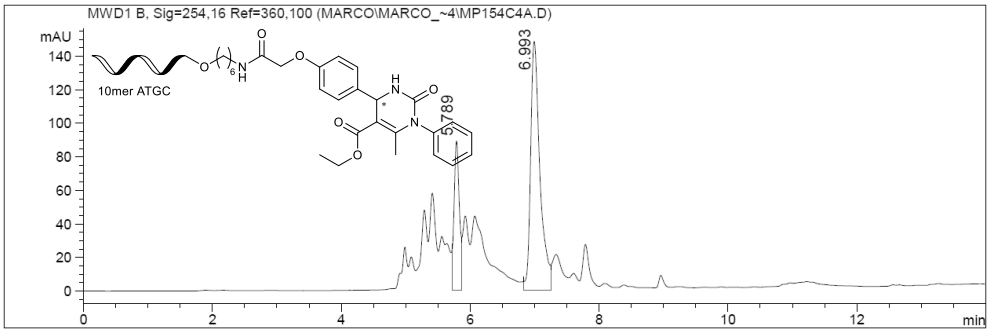
Ret. Time	Width min	Height	Area	Area %
6.348	0.135	42.897	346.906	13.444
6.555	0.171	218.316	2233.427	86.556

MALDI-MS spectrum of isolated product 27b



DNA conjugate 27c: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with *N*-phenylurea **24c** and ethyl acetoacetate **25** according to RP-10.

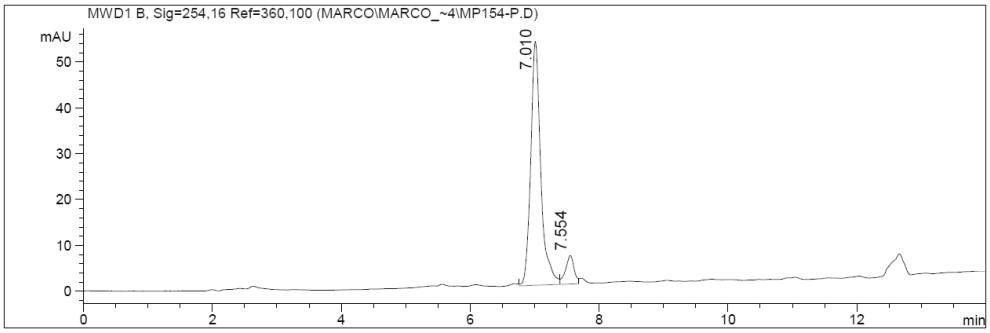
HPLC trace of crude reaction mixture 27c (Analytical RP-HPLC, Method-III)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.789	0.095	89.395	508.282	25.470
6.993	0.167	148.519	1487.302	74.530

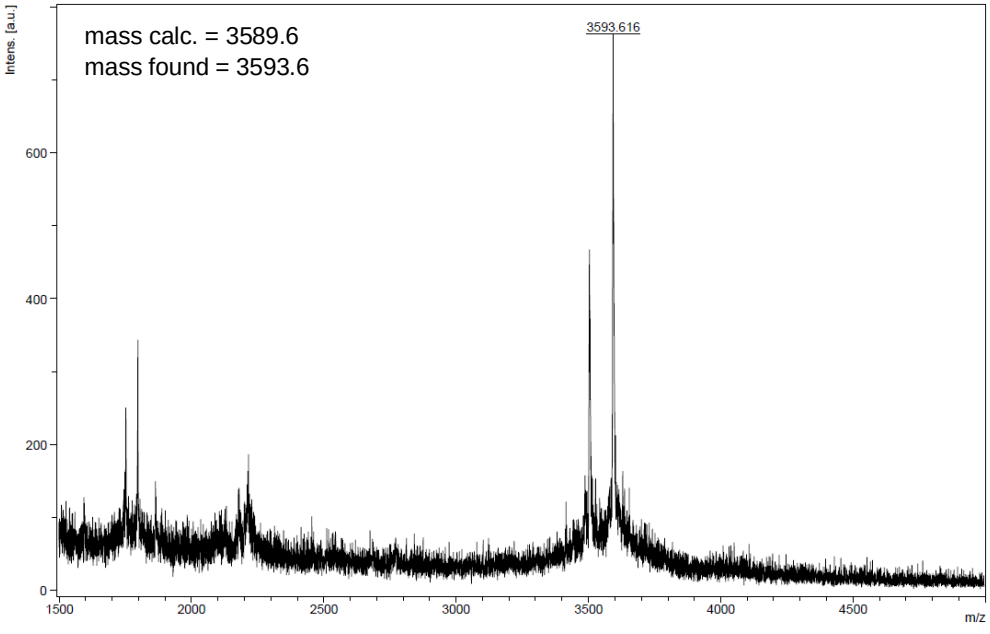
HPLC trace of isolated product 27c (Analytical RP-HPLC, Method-III)



Peak list:

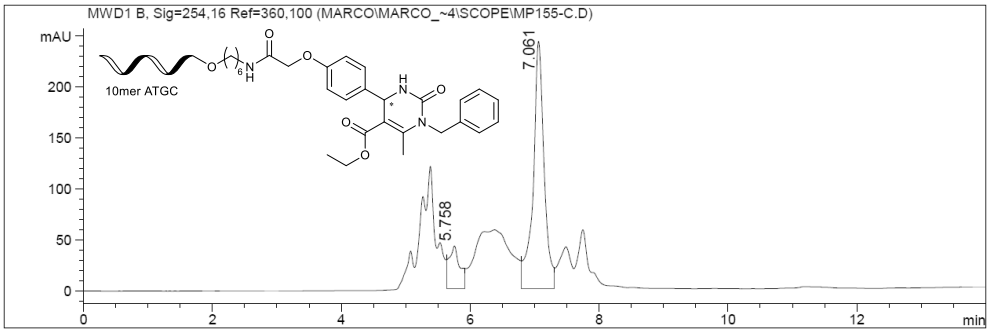
Ret. Time	Width min	Height	Area	Area %
7.010	0.159	53.187	577.659	91.044
7.554	0.133	6.209	56.827	8.956

MALDI-MS spectrum of isolated product 27c



DNA conjugate 27d: CPG-coupled 10mer ATGC-aldehyde conjugate **15a** was reacted with *N*-benzylurea **24d** and ethyl acetoacetate **25** according to RP-10.

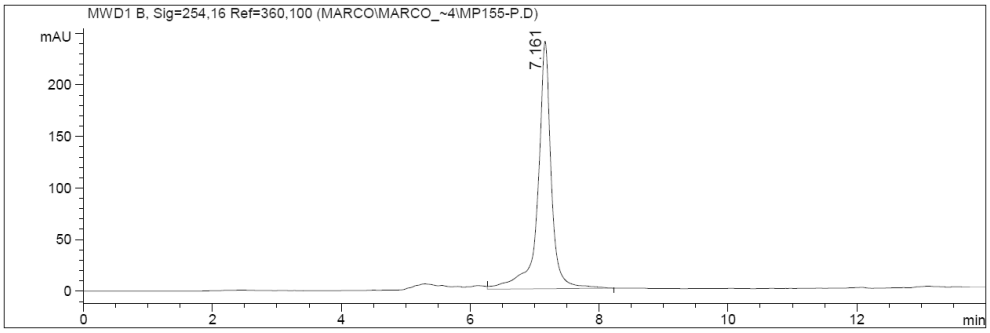
HPLC trace of crude reaction mixture 27d (Analytical RP-HPLC, Method-III)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.758	0.200	42.105	504.256	15.058
7.061	0.195	242.740	2844.499	84.942

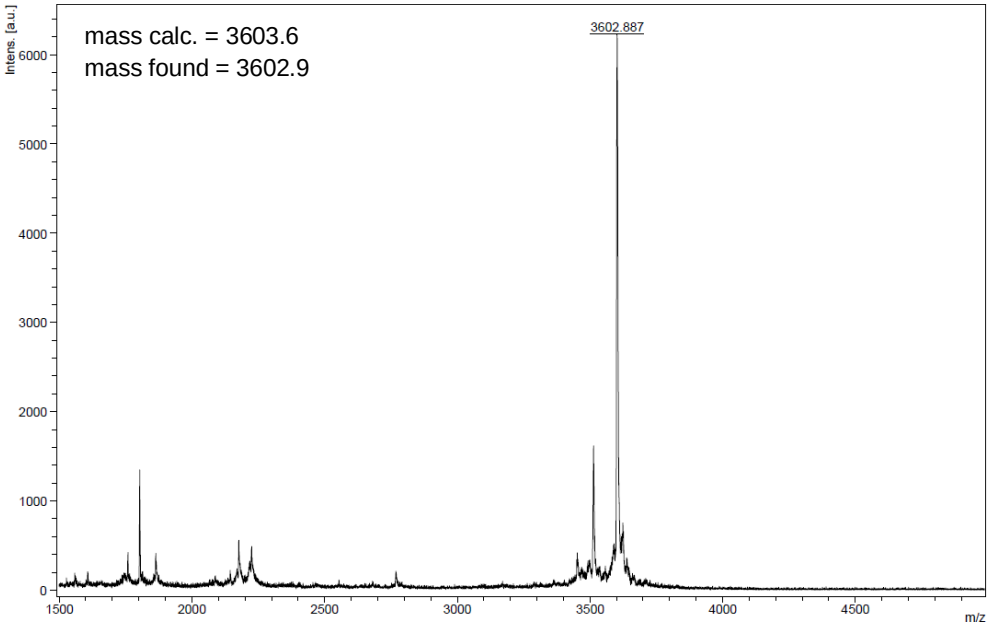
HPLC trace of isolated product 27d (Analytical RP-HPLC, Method-III)



Peak list:

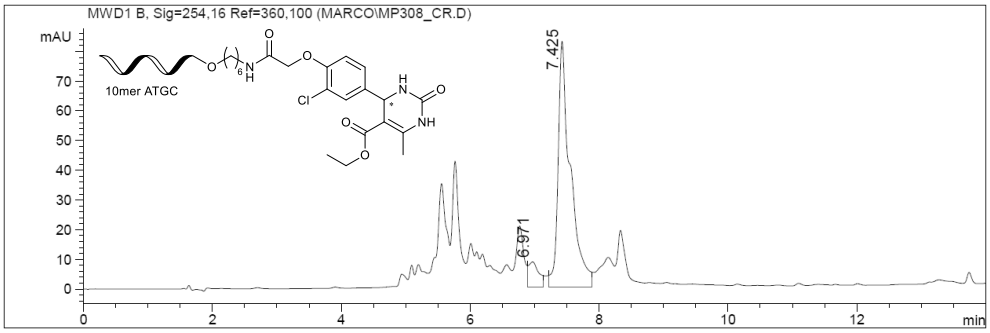
Ret. Time	Width min	Height	Area	Area %
7.161	0.206	240.100	3503.402	100.000

MALDI-MS spectrum of isolated product 27d



DNA conjugate 27e: CPG-coupled 10mer ATGC-aldehyde conjugate **15b** was reacted with urea **24a** and ethyl acetoacetate **25** according to RP-10.

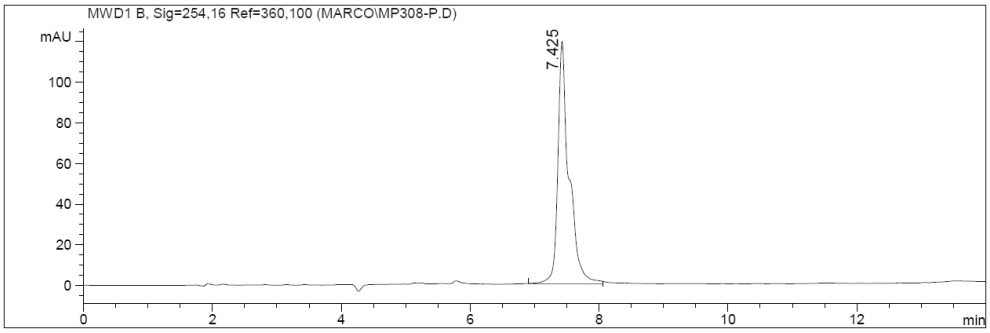
HPLC trace of crude reaction mixture 27e (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
6.971	0.178	8.538	91.303	7.685
7.425	0.221	82.818	1096.778	92.315

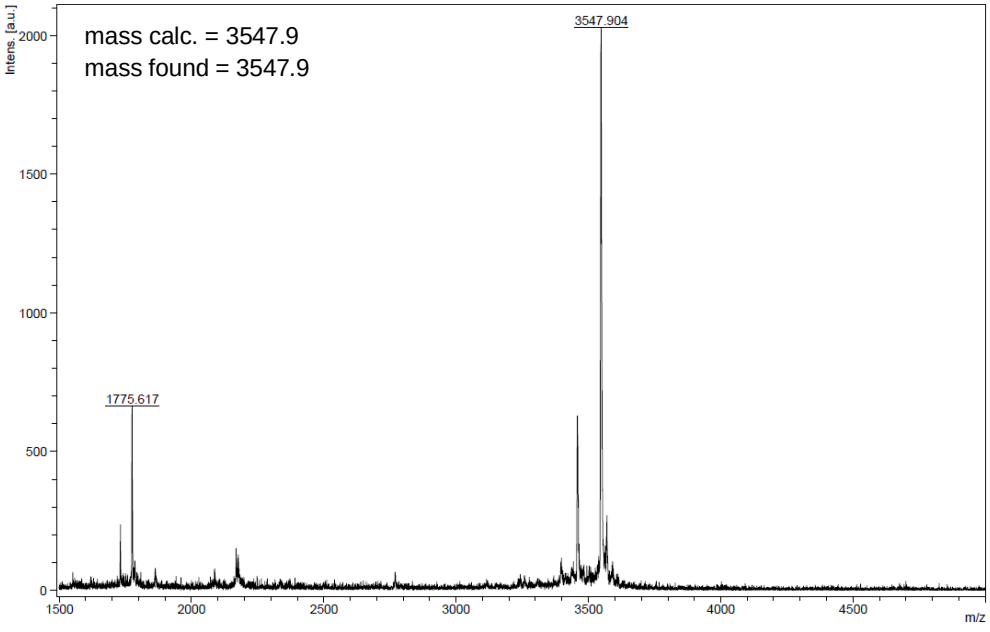
HPLC trace of isolated product 27e (Analytical RP-HPLC, Method-II)



Peak list:

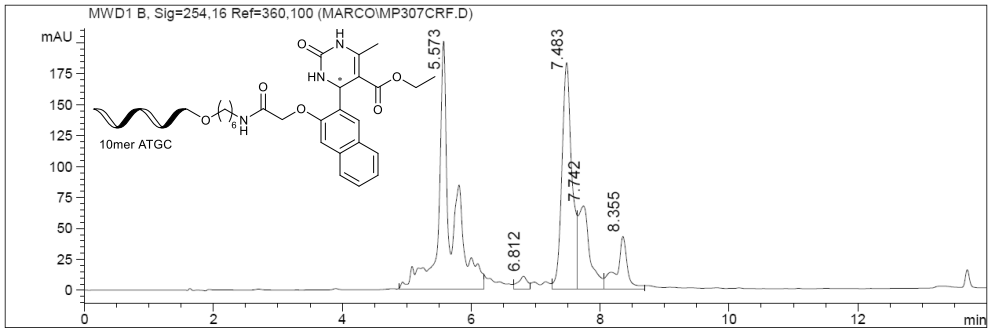
Ret. Time	Width min	Height	Area	Area %
7.425	0.199	119.402	1425.893	100.000

MALDI-MS spectrum of isolated product 27e



DNA conjugate 27f: CPG-coupled 10mer ATGC-aldehyde conjugate **15c** was reacted with urea **24a** and ethyl acetoacetate **25** according to RP-10.

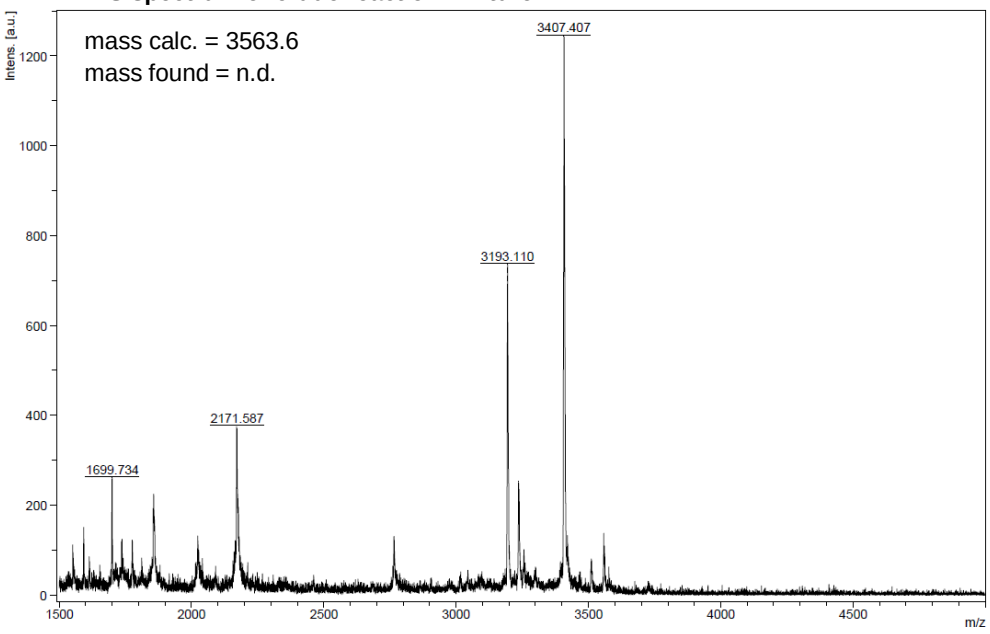
HPLC trace of crude reaction mixture 27f (Analytical RP-HPLC, Method-II)



Peak list:

Ret. Time	Width min	Height	Area	Area %
5.573	0.235	201.018	2834.301	45.431
6.812	0.165	10.104	100.238	1.607
7.483	0.179	183.128	1969.024	31.561
7.742	0.208	66.999	834.551	13.377
8.355	0.197	42.426	500.637	8.025

MALDI-MS spectrum of crude reaction mixture 27f



Cheminformatic analysis

For library design, characterization and analysis the software KNIME[1] was used, with the following implemented extensions: RDKit, Indigo, ChemAxon, CDK, Vernalis.[2]

As a source database for the components required for the reactions, the Aldrich Market Select database (AMS)[3] was used and split in order to retrieve the different compound classes according to functional groups. Prior to the library design, the molecules in the AMS database were firstly standardized and filtered by molecular weight and number of unspecified stereocenters by RDKit Descriptor Calculation: the threshold was set to 200 Da for each compound class to ensure a reasonable size of the final product. In order to retrieve the different building block classes from the AMS, the RDKit Functional Group Filter or the Indigo node Substructure Match Counter combined with the Rule-based Row splitter were used, defining the substructure or the further filters by the ChemAxon Marvin Sketch node. We removed all aldehyde building blocks that contain the carboxylic acid moiety and/or bulky groups in *ortho* position to the carboxaldehyde and kept this compound class constant for the DA-1, P and B libraries. Further specific filters were applied to each compound class per each library depending on the experimental reactivity or on the presence of further functional groups which might lead to cross-reactivity. For the DA-1 library we removed heteroaromatic amines and anilines substituted with bulky *ortho*-substitution. For the DA-2 library, anilines with carboxylic acid amide or bulky groups in *ortho*-position were excluded, yet, all available aldehydes were included in the analysis. For the Povarov library the hetero-aromatic amines were filtered out. For the Biginelli library, differently substituted ureas and β-ketoesters were used, but, in order to obtain libraries of comparable compound numbers, a further molecular weight filter was applied to starting materials (170 Da for ureas and esters) and products (450 Da).

All the building block classes were submitted to the RDKit Catalog filter node in order to remove compounds with unwanted reactivity.[4] For computational reasons and in order to obtain libraries of comparable sizes, larger building block datasets were sampled to 1000 molecules with the RDKit diversity picker (aldehydes and anilines). The reactions required for the *in silico* libraries were designed using a combination of RDKit node Two Component Reaction or Chemical Transformation, the Chemaxon Marvin Sketch for the reaction scheme and the SDF Files Reader for the different components. From the Enamine REAL database[5], 500000 molecules were randomly sampled to obtain comparable data sets. We calculated the MQN descriptors for each compound of each library with the node RDKit Descriptors Calculation and, after Min-max normalization among the concatenated data of the libraries and the commercially available molecules, the PCA values were plotted in 3D scatter plots (Figure S3) using the Gnuplot[6] script, to visualize chemical diversity.

The PMIs were calculated with the corresponding Vernalis node, based on the 3D coordinates generated by RDKit Generate Coords node, to evaluate library shape diversity (Figure S4).

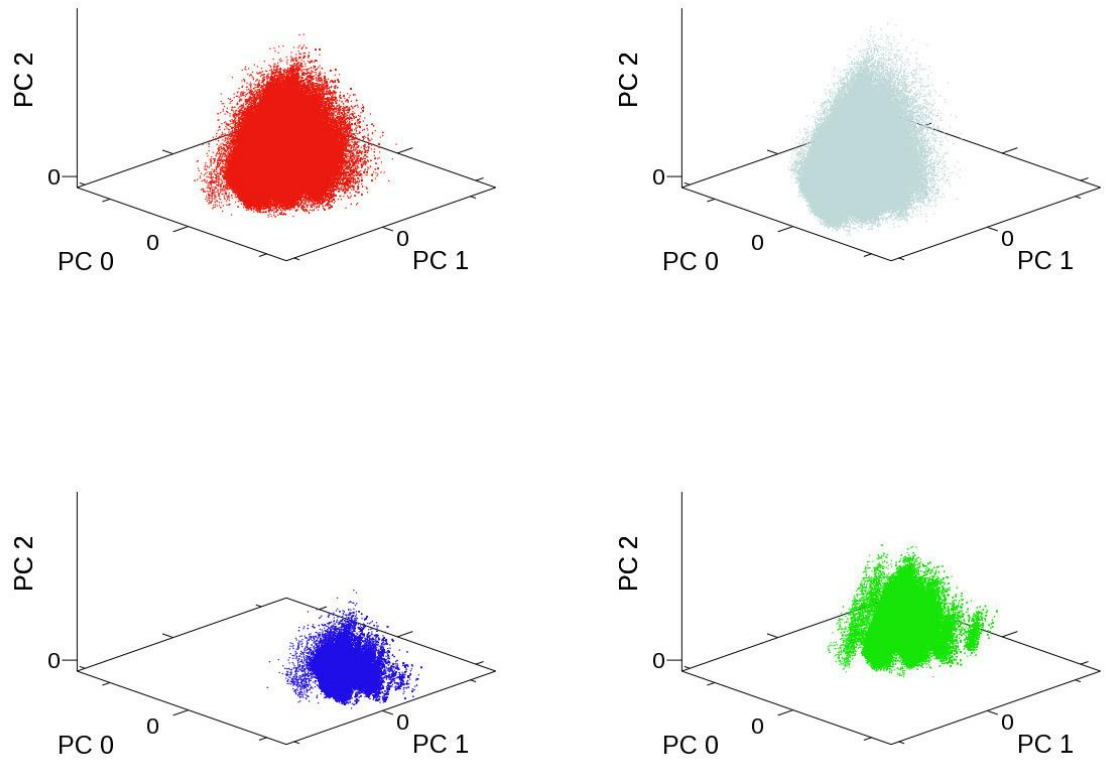


Figure S3 PCA plots of the DA-1 (red), Enamine REAL sampled database (grey), P (blue) and B (green) libraries.

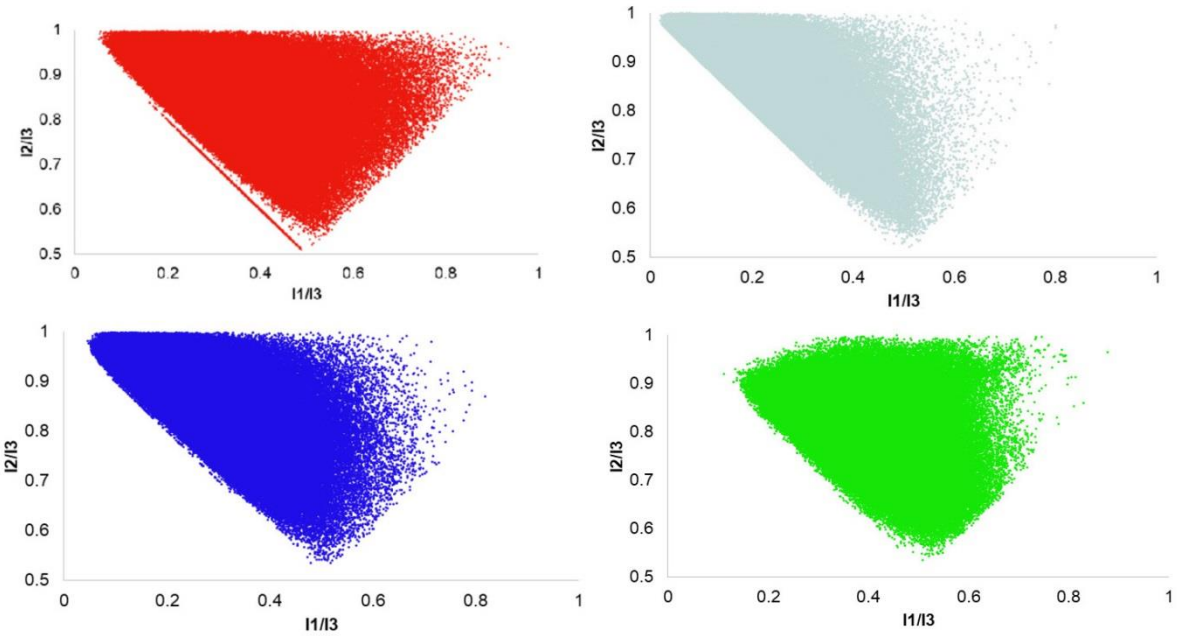


Figure S4 PMI plots of the DA-1 (red), Enamine REAL sampled database (grey), P (blue) and B (green) libraries.

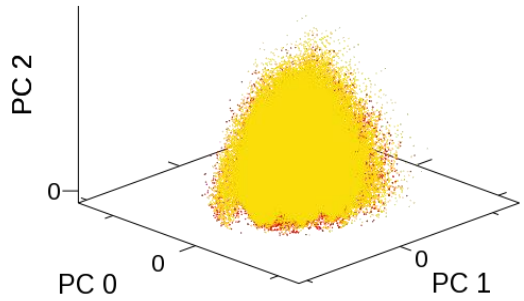


Figure S5 PCA plots of the DA-1 (red) and DA-2 (yellow) libraries, covering almost identical chemical space.

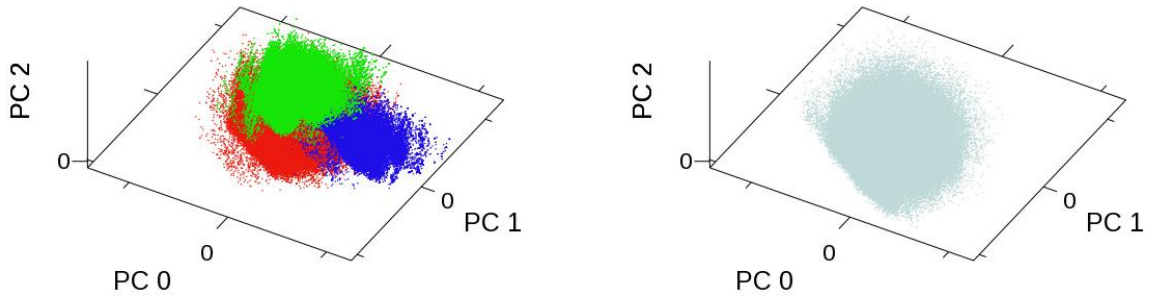


Figure S6 PCA plots of the combined DA-1 (red), P (blue) and B (green) libraries vs Enamine REAL sampled database (grey), viewed from a different perspective.

References:

1. https://www.knime.com/downloads
2. M. P. Mazanetz, R.J. Marmon, C. B.T. Reisser, I. Morao, Curr. *Top. Med. Chem.,* 2012, **12**, 1965-1979.
3. https://www.sigmaaldrich.com/chemistry/chemistry-services/aldrich-market-select.html
4. J. B. Baell, J. W. M. Nissink, *ACS Chem Biol.* 2018, **13**, 36-44.
5. https://enamine.net/library-synthesis/real-compounds/real-compound-libraries
6. http://gnuplot.info